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Abstract Volume

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Time	Sunday Aug 24	Monday Aug 25	Tuesday Aug 26	Wednesday Aug 27	Thursday Aug 28
8:00		REGISTRATION	REGISTRATION	REGISTRATION	REGISTRATION
8:30		PANG, DUNKLEY & JETLY Symposium 1 Room 200D QURAAN Symposium 2 Room 200C	GAETZ ISACM Symposium 3 Room 200D KNAPPE, SANDER & PARKKONEN Symposium 5 Room 200C	GRAMFORT Symposium 12 Room 200D HERNANDEZ-PAVON & SARASSO Symposium 13 Room 202 BAHRAMI-SHARIF & BAILLET Symposium 14 Room 200C	DAFFERTS-HOFER Symposium 18 Room 202 DELLA PENNA Symposium 19 Room 200C ROSS & JOHNSON Symposium 20 Room 200D
9:00					
9:30					
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10:30		COFFEE BREAK	COFFEE BREAK	COFFEE BREAK	COFFEE BREAK
11:00		Dr. R. Hari Keynote Lecture	Dr. E. Halgren Keynote Lecture	Dr. G. Barnes Keynote Lecture	Dr. O. Jensen Keynote Lecture
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12:00		Lunch with Poster Session 1	Lunch with Poster Session 2	Lunch with Poster Session 4	Lunch Zimmerman prize award Bussiness Meeting
12:30			Data Comp		
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13:30					COFFEE BREAK
14:00	REGISTRATION	NAKASATO ISACM Symposium 1 Room 200D JERBI & SINGH Symposium 3 Room 200C	WIEKHORST Symposium 6 Room 202 JOUSMAKI & DE TIEGE Symposium 7 Room 200D LINA & CARRIER Symposium 8 Room 200C	Hot Topics and Zimmerman prize talk Room 200D KIM Symposium 15 Room 200C	LITVAK & BUTZ Symposium 21 Room 200C BAUMGARTEN Symposium 22 Room 202 SHIRASHI Symposium 23 Room 200D
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18:00	Dr. P. Morris Opening Keynote				
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Keynotes

K1: MULTIMODAL NEUROIMAGING: INTEGRATION OF MEG, FMRI AND MRS APPROACHES

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There is spatial co-localization of the evoked responses measured by MEG and the haemodynamic response to neural activation measured by functional MRI (fMRI). It has also become well-established that the same spatial correspondence exists for the induced neuro-oscillatory responses (ERS and ERD). Some of these, for example the gamma band response in the visual cortex, show a high correlation with fMRI measures of neural activity.

FMRI has established the presence of functional brain networks, in the 'resting state' and during task performance. These same networks are found in MEG data, most strongly in the beta band. Their independent observation by MEG and fMRI suggests they play an important role in the hierarchical organization of the brain and as such will be a primary focus of future research. MEG will be central because it reveals the temporal dynamics between and within networks.

The neural oscillations that underpin network activity are controlled in a balance between excitatory and inhibitory inputs mediated by the principal excitatory and inhibitory neurotransmitters, glutamate and GABA, respectively. It is now possible, using 1H MRS, to measure their concentrations together with those of other neurometabolites such as glutamine and glutathione. To what extent they reflect excitatory/inhibitory activity is a matter of debate. However, the measurement of neurotransmitter cycling rates using 13C MRS should help to resolve this issue.

The techniques discussed in this lecture will be illustrated with results from an ongoing study of schizophrenia in which highly significant differences in salience network activity have been observed in the processing of relevant/irrelevant stimuli, together with differences in neurometabolite levels in the nodes of this and other networks.

K2: BRAIN IMAGING OF SOCIAL INTERACTION – WHY AND HOW?

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We are embedded in social interaction—teaching, learning, communicating, treating, deceiving, and punishing—to that extent that other people as "person stimuli" have a central role in our lives. Importantly, we are actively participating in interaction rather than only observing and reacting. To fully understand such interactive aspects of human brain function we might shift to two person-neuroscience, which considers a dyad rather than an individual as the proper analysis unit and aims to image the interacting person's brains at the same time in as real-life-like conditions as possible. Dual-brain imaging, despite its conceptual advantages, still has multiple experimental and analysis challenges to be solved.

K3: WHAT IS THE N400M?

HALGREN, Eric, Radiology, Neurosciences and Psychiatry, University of California San Diego, San Diego, USA
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The N400m connects synaptic activity in particular times and places with lexico-semantic processing. Where does it come from? Does everybody have one? When does it develop? Does it have a critical period? What does it do? What comes before, and after it? Is there one N400m or many? How is it related to spontaneous rhythms? How is it related to non-language processing? Is it a species-specific form of object recognition? I will address these questions with the results of MEG and intracranial recordings.

K4: MORE STRUCTURE MORE FUNCTION

BARNES, Gareth, Wellcome Trust Centre for Neuroimaging, University College London, London, UK
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The MEG data we measure are due to an interaction between cortical structure and function. Typically we take structure (grey matter) to be known and attempt to reconstruct function (current flow). This problem is ill-posed and so different functional assumptions about how the brain might work (sparse or distributed, correlated or uncorrelated sources) give rise to different functional estimates. The problem is that we almost never know the functional ground truth. Typically therefore we use metrics like model evidence- which balances the amount of data explained by a functional estimate with its complexity- to judge between solutions.

An alternative is to turn the problem around and pretend that the functional assumptions are known and attempt rather to reconstruct the anatomy. The advantage here is that we know the anatomical ground truth (where the grey matter lies). If our functional assumptions are groundless we will have no chance of recovering the grey matter structure; if however our functional assumptions have some validity then our anatomical estimates should match the true brain structure.

There are many applications of this approach. I will begin by talking about how we can use it to factor out errors in co-registration. I will then go on to get a measure of functional accuracy by seeing how much one has to distort a brain before it becomes an unlikely model. Finally I will talk about how we can use these models of structure to distinguish between functional contributions from deep versus superficial cortical laminae.

K5: LINKING MECHANISM TO BEHAVIOR: NEURONAL OSCILLATIONS PROVIDE A MECHANISM FOR PRIORITIZING SENSORY PROCESSING

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When operating in natural environments our brains are bombarded with information. As such our sensory systems must rely on powerful attentional mechanisms to prioritize the inputs. We and others have applied MEG to demonstrate that regionally specific neuronal oscillations in the alpha band are intimately involved in prioritizing information processing by suppressing irrelevant input. Further, feed forward processing is reflected by gamma band activity physically modulated by the alpha rhythm. Both ADHD patients and aging adults are impaired in modulating these oscillations. Using MEG in combination with fMRI, TMS and DTI we have uncovered parts of the network controlling the posterior rhythms. In particular the frontal-eye field plays a strong role in exercising top-down control via the superior longitudinal fasciculus. Finally we have developed a new framework implemented at as a computational model making explicit how the phase of the alpha oscillations could organize a temporal code prioritizing visual processing. In conclusion, MEG in combination with other techniques provides an excellent opportunity for uncovering the mechanistic underpinnings of behavior.

Jensen, O., Gips, B., Bergmann, T.O. and Bonnefond, M. (2014) Temporal coding organized by coupled alpha and gamma oscillations prioritize visual processing. Trends in Neurosciences 37(7):357-369.

Symposia

S1: MEG AS A DIAGNOSTIC TOOL FOR POST-TRAUMATIC STRESS DISORDERS IN MILITARY COMBATANTS

CHAIRS:

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Post-traumatic stress disorder (PTSD) is a psychiatric condition that has been receiving increasing attention. It is estimated that 30% of individuals who have spent time in war zones, and 10% of the general population, will experience PTSD. PTSD often presents with co-morbidities making differential diagnosis difficult. The application of MEG to the study of PTSD has been promising. The temporal and spatial resolution of MEG, as well as its ability to look at responses in both the time and frequency domains, has raised the possibility that MEG might have the sensitivity and specificity to be used as a neuroimaging biomarker for PTSD.

The speakers within this symposium will present their work on the applications of MEG to military PTSD populations. The topics will cover MEG measures of neural synchrony, connectivity, resting state source magnitude images, and task-based cognitive deficits as it pertains to PTSD. As well, multi-modal investigations using MEG, DTI, and MRI will be presented.

This symposium is timely and highlights a novel application of MEG to a prevalent and debilitating clinical condition. This symposium will draw broad interest from both basic researchers interested in cutting-edge, integrative MEG methods and clinicians who work with patients with PTSD.

MODULATION OF SYNCHRONOUS NEURAL INTERACTIONS (SNI) WITH TRAUMA AS REVEALED BY MAGNETOENCEPHALOGRAPHY

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The synchronous neural interactions (SNI) test which assesses the functional interactions among neural populations derived from MEG recordings can successfully differentiate PTSD patients from healthy control subjects. The main differences in cortical communication circuitry between these two groups lie in the miscommunication of temporal and parietal and/or parieto-occipital right hemispheric areas with other brain areas. This lateralized temporal-posterior pattern of miscommunication was very similar but was attenuated in patients with PTSD in remission. In an extension of these studies to brain adaptation to traumatic events, we found that SNIs were significantly modulated downward with increasing lifetime trauma scores in resilient control veterans but not in veterans with PTSD. This effect, which was primarily characterized by negative slopes (i.e., decorrelations) in small neural networks, was strongest in the right superior temporal gyrus. Significant negative slopes were more common, stronger, and observed between sensors at shorter distances than positive slopes in both hemispheres for controls, but not for PTSD. In conclusion, neural modulation involving decorrelation of neural networks in the right superior temporal gyrus, and to a lesser extent other areas, distinguishes resilient veterans from those with PTSD and is postulated to play an important role in healthy response to trauma.

DEVELOPING MEG AND DTI MARKERS FOR PTSD

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Post-traumatic stress disorder (PTSD) is a leading cause of sustained cognitive, emotional, and behavioral deficits, in military personnel, veterans, and the general population. Although much progress has been made, the neuro-physiological changes in PTSD are not well understood, and PTSD symptoms often overlap with those from mild traumatic brain injury (mTBI). Conventional neuroimaging techniques such as MRI and CT have limited sensitivity in detecting physiological abnormalities caused by PTSD. Here, we examined resting-state MEG activity in patients with PTSD. Compared with healthy control subjects, PTSD patients showed hypo-activity in delta, theta, and alpha bands. However, for beta and gamma bands, PTSD patients showed hyperactivity in the “fear network” involving amygdala and dorsal aspect of cingulate cortex. In the meantime, patients with PTSD also showed hypoactivity in medial-inferior frontal area also in beta and gamma bands. This study is probably the first MEG source imaging research revealing hyperactivity in “fear network” and hypoactivity in medial-inferior frontal area, consistent with reduced frontal inhibition to the “fear network” in PTSD. We will also present results showing reduced fractional anisotropy (FA) in white matter tracts using diffusion tensor imaging (DTI). Furthermore, we will discuss potentials of using MEG to differentiate PTSD from mTBI.

CONNECTIVITY STRENGTH IN MEMORY STRUCTURES CORRELATES WITH SYMPTOM-SPECIFIC OUTCOMES IN PTSD VETERANS

DUNKLEY, Benjamin T., Hospital for Sick Children, Toronto, Canada
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Post-traumatic stress disorder (PTSD) is a serious psychiatric condition characterized by anxiety which manifests after experiencing a traumatic life event. Whilst its psychological causes and resultant symptomology are well understood, relatively little is known about potential changes in neurophysiology. In particular, there is a lack of knowledge whether changes in functional connectivity may be linked to the disorder. Here, using non-invasive neuroimaging with magnetoencephalography, we identify atypical resting state associated with PTSD in veterans. Specifically, we show that the resting state oscillatory coherence in a combat-related PTSD population expressed long-range hyperconnectivity in the gamma band largely confined to the left temporal and frontal regions when compared to those who underwent comparable experiential events but did not develop PTSD. Additionally, we show that the importance of network nodes in certain regions (defined by strength within the atypical network) correlates with

cognitive-behavioural outcomes. Importantly, we uniquely demonstrate that hippocampal hyperconnectivity in the PTSD group is associated with PTSD symptom severity. Given this, we conclude that these atypical synchronous neural interactions may underlie some of the psychological symptoms of PTSD, and that the hyperconnectivity in memory-related regions with other nodes in the aberrant network contributed to abnormal brain function underlying the symptoms of PTSD.

POST-TRAUMATIC STRESS DISORDER AND ITS IMPACT ON SET-SHIFTING

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Individuals affected by PTSD complain of a number of cognitive symptoms including difficulties with mental flexibility. Mental flexibility underlies the ability to adapt to changing situations and respond to new information. Neuroimaging studies of mental flexibility use a set-shifting task where the participant is required to select a correct response based on a set of implicit rules. During the task, the rules change, and the participant is required to 'shift' and select responses based on the new rules.

Soldiers with and without PTSD, as well as a group of civilians, participated in a MEG study using a set-shifting task. Compared to control soldiers and civilians, the soldiers with PTSD were slower and less accurate when shifting sets. As expected, the civilians recruited lateral inferior frontal regions and bilateral insulae when shifting. The PTSD group recruited these areas, as well as additional areas in parietal and temporal cortices. Furthermore, the PTSD group showed higher magnitude activations compared to both the civilian and control soldier groups. Thus, despite greater neural activation and increased recruitment of supporting brain regions, the soldiers with PTSD perform more poorly on a set-shifting task. This finding may be related to the difficulties with mental flexibility seen in PTSD.

NETWORKS, NOISE AND PTSD

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The effects of posttraumatic stress disorder (PTSD) are thought to be diffuse, involving a wide range of areas and projections in the brain. This suggests the possibility that PTSD phenotypes may be expressed as disturbances in information processing at the large-scale, system level. In this talk I will explore the utility of two complementary measures of neural function to study PTSD: global connectivity and brain signal variability. To determine how global information transfer is affected by PTSD, partial least squares (PLS) analysis was used to isolate multivariate patterns of functional connections that optimally differentiate soldiers with and without PTSD. To determine how PTSD affects the rate at which information is generated by individual brain regions, the variability of neural activity was estimated using multiscale entropy (MSE) analysis. Together, these results reveal that PTSD affects both the generation and transfer of information in brain networks.

S2: NETWORK DYSFUNCTION IN NEUROLOGICAL AND PSYCHIATRIC DISORDERS: WHAT HAVE WE LEARNED?

CHAIR:

QURAAN, Maher, TWRI, Toronto, Canada
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The study of the human brain as a functional network has led to tremendous insight into the function of the healthy brain and the different kinds of impairments that can lead to brain dysfunction in various neurological and psychiatric disorders. A wide range of synchronization measures have been used to study functional connectivity in EEG and MEG. However, most such measures suffer from tremendous methodological limitations complicating the interpretation of connectivity results. In this symposium we will assess synchronization measures and focus on their ability to characterize functional impairments associated with neurological and psychiatric disorders including epilepsy, depression, autism spectrum disorder, gliomas, Parkinson's disease and Multiple Sclerosis. The speakers will summarize what we have learned so far regarding these diseases and discuss consistent as well as conflicting evidence, thus, highlighting what has been achieved and what is yet to be learned. The application of graph theory will also be discussed in the context of understanding changes in network properties associated with such disorders and the methodological challenges associated with graph theory including thresholding and normalization.

BIASES IN BRAIN NETWORK ANALYSES: DOES THE MINIMUM SPANNING TREE PROVIDE A SOLUTION?

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Magnetoencephalography can be used to characterize the functional brain networks that are formed by interacting sources of oscillatory activity. First, we reconstruct the time-series of active regions using an atlas-based beamforming approach, following which functional interactions are estimated using the Phase Lag Index (PLI), a measure that is insensitive to the effects of field spread and volume conduction. The topology of the functional networks that are formed by these interacting regions can subsequently be characterized using graph theoretical tools. However, it is not trivial to compare network topology across individuals, groups, studies or modalities, since many network properties depend on the size and average degree (number of connections/region) of the network. Commonly used solutions, such as setting a threshold to fix the number of nodes and average degree, do eliminate size effects but may exuberate the influence of noisy connections or ignore strong connections. Similarly, using random surrogates for normalization may also introduce biases. In this talk I will argue that computation of the minimum spanning tree allows for a bias-free reconstruction of the core of the functional networks. Application of this approach will be illustrated through examples from recent studies in patients with gliomas, Parkinson's disease, and Multiple Sclerosis.

EPILEPSY SURGERY OUTCOME AND FUNCTIONAL NETWORK ALTERATIONS IN LONGITUDINAL MEG: A MINIMUM SPANNING TREE ANALYSIS

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Epilepsy is common in patients with circumscribed brain abnormalities, such as primary brain tumors and mesiotemporal sclerosis. In a substantial number of patients, anti-epileptic drug treatment is ineffective, and many of these patients are referred to epilepsy surgery programs. Unfortunately, seizure freedom after resective epilepsy surgery is not obtained in a substantial number of patients. Functional connectivity and network analyses may be promising techniques to reach a better understanding of the pathophysiology of lesional epilepsy, and may even be used for more accurate identification of the target areas for epilepsy surgery. Regions that can be resected to obtain seizure freedom, the so-called epileptogenic zone (EZ), seem to have a role as pathological hubs in the functional brain network. The use of network analysis in combination with source-space MEG recordings may provide a non-invasive method for identification of the EZ. However, methodological limitations have so far hampered implementation of these techniques in clinical practice. Minimum spanning tree (MST) network analysis provides a bias-free approach to capture the most important connections in the network that may be used for more accurate characterization of the EZ. I will describe how MST characteristics are altered by surgical intervention in relation to post-operative seizure freedom.

OSCILLATORY NETWORK PLASTICITY IN SCHIZOPHRENIA AND STROKE

NAGARAJAN, Srikantan, Director, Biomagnetic Imaging Laboratory, University of California, San Francisco, USA
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In this talk, I will focus on novel magnetoencephalographic (MEG) imaging methods for assessing functional activations and connectivity with applications to neurological and psychiatric disorders. First, I will review recent imaging studies from my research group in patients with schizophrenia. We have documented abnormal functional activations, brain-behavior correlations and functional connectivity in patients with schizophrenia. We have also found computerized training induced plasticity in these patients. Second, I will review imaging studies of resting-state functional connectivity in stroke patients where we demonstrate functional biomarkers of brain plasticity and of behavioral recovery. These studies highlight the power of MEG imaging to examine brain networks alterations in neurological and psychiatric disorders.

REDUCED NETWORK COHERENCE IN AUTISM: EMERGING PERSPECTIVES ACROSS AGE AND TASK

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Coherent neural oscillations are thought to mediate communication among brain regions, supporting cognitive and perceptual dynamics. Disruption of synchronization in distributed networks is associated with numerous neurological and psychiatric conditions. The present talk will review recent findings of reduced task-dependent MEG phase synchronization in distributed brain networks in autism spectrum disorder (ASD) across several tasks. We investigated source-resolved phase locking among distributed brain regions in children, adolescents and adults with ASD. Paradigms targeting core deficits in mental flexibility, social cognition and holistic processing were used. Specifically, we performed synchronization analysis in children who performed an executive set-shifting task, adolescents during the perception of emotional faces, and adults who were engaged in a numerosity estimation paradigm. These studies indicated reduced functional connectivity among task-relevant brain areas in ASD across age groups and across tasks. Such findings underscore the value of assessing population-relevant task-based connectivity and suggest that reduced communication in specific brain networks may contribute to social and cognitive difficulties prevalent in ASD. These results are in agreement with the view that disordered synchronization of neural oscillations contributes to dysfunctional neural network dynamics in clinical populations.

FUNCTIONAL CONNECTIVITY AND GRAPH THEORY IN EEG AND MEG AND APPLICATION TO TEMPORAL EPILEPSY AND DEPRESSION

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Functional connectivity has shown great promise in elucidating brain function at the network level. In EEG and MEG, various synchronization measures have been used to estimate functional connectivity in sensor space and source space. In this presentation we will focus on two recent clinical EEG studies employing functional connectivity and graph theory to characterize neurological and psychiatric disorders. In the first study (Quraan et al. 2013a) we investigated EEG resting state data recorded from 12 patients with treatment resistant depression that have undergone DBS surgery; of those, six patients were classified as responders to DBS. Results showed differences in mean hemispheric asymmetry between responders and non-responders as well as differences in long-range frontal-parietal connectivity. In the second study (Quraan et al. 2013b), resting state data from patients with temporal lobe epilepsy revealed significantly higher synchronization than controls in low frequency bands, but lower synchronization in high frequency bands. Deviations from the optimal small world network architecture were also observed. Finally, we highlight the challenges that remain for understanding connectivity in source space using MEG (Quraan et al. submitted) and propose a way forward for better characterization of connectivity in source space.

ISACM S1: CURRENT STANDARD OF CLINICAL CARE

CHAIR:

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EPILEPSY THEORY AND GROUNDING

NAKASATO, Nobukazu[1], RAMPP, Stefan[2], *(1) Department of Epileptology, Tohoku University School of Medicine, Sendai, Japan (2) Department of Neurology, Epilepsy Center, University Hospital Erlangen, Germany*
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MEG analysis and especially source localization in patients with epilepsy is now widely accepted as a part of the clinical routine. It yields valuable clinical information and enables patients to proceed to epilepsy surgery who would not have been eligible candidates without this information. Vice versa, patients are identified early who are unlikely to benefit from surgery. Even screening applications utilizing MEG are being discussed.

This presentation will provide an introduction to the field of epileptology in the context of clinical MEG. Basic pathomechanisms, etiologies and clinical presentations are reviewed. Using case examples, an overview is given about typical diagnostic and therapeutic options, as well as their practical implementation. Electrophysiological markers, from conventional spikes and seizures to novel infra-slow and fast activity patterns are summarized. Finally, the current shortcomings, open questions and problems are addressed, to the solution of which MEG and novel signal analysis techniques may contribute in the future.

SENSITIVITY AND SPECIFICITY OF SEIZURE-ONSET ZONE ESTIMATION BY ICTAL MEG

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Magnetoencephalography MEG is a robust non-invasive method for localizing sources of epileptic brain activity. Together with other non-invasive methods, such as ictal video-EEG, brain magnetic resonance imaging (MRI), 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography (PET), and ictal single-photon emission computed tomography (SPECT), MEG is used to localize the epileptogenic area to be removed in order to treat pharmacoresistant epilepsy. Exploration with intracranial EEG subdural electrode grids and/or stereotactically implanted depth electrodes (SEEG) is often still needed to confirm or delineate the epileptogenic zone. Inter-ictal MEG spikes are easy to analyze with dipoles, and the location of a dipole cluster may be associated with ictal onset zone, and thus increase the probability of successful seizure-onset zone targeting by intracranial EEG (Iida et al. 2005). The diagnostic efficacy of inter-ictal MEG compared to ictal ICEEG has a positive predictive value of 80-90% (Knowlton et al. 2006). When the relative prognostic values of non-invasive diagnostic methods were compared with seizure-onset location by ICEEG, gains in diagnostic yield were seen only in combinations containing MEG (Knowlton et al. 2008). MEG results changed the treatment decision in one third of patients, and were crucial for successful surgery outcome in 10% (Sutherling et al. 2008).

Most studies of the diagnostic efficacy of MEG are based on inter-ictal spikes.

Prediction of seizure onset zone by ictal and interictal MEG dipoles were compared to ictal ICEEG (subdural grid recordings). The specificity and sensitivity of the prediction were calculated at lobar and sublobar surface resolution. The sensitivity of ictal MEG was 96% on lobe level and 70% on surface level, and its specificity was 90 % on lobe level and 73 % on surface level. The sensitivity of an inter-ictal cluster was similar on lobe but lower (40 %) on surface level. The specificities of the inter-ictal cluster and ictal dipoles were similar (73-90 %) (Medvedovsky et al. 2012). The classical dipole analysis requires a sufficient signal-to-noise ratio, which is not always the case at seizure onset. Therefore other methods, e.g., a beamformer-based delineation of a spiking volume (Bouet et al 2012) may also show value in localizing the generators of ictal onset rhythms (Jung et al. 2013).

Despite statistical challenges, sensitivity and specificity of ictal MEG results appear close to those of inter-ictal results, which seem to agree regardless method of source analysis, MEG hardware, or epilepsy surgery center. MEG appears to bring true additional value to the presurgical planning of epilepsy surgery candidates.

CLINICAL CHALLENGES IN PEDIATRIC EPILEPSY: ROLE OF MEG

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Abstract: Pediatric patients with medically intractable epilepsy present unique challenges, due to unique aspects of the developing brain. The developmental defects and syndromes that present in infancy or childhood often result in intractable focal or regional epilepsies. These aspects in turn contribute to the sometimes conflicting or complex data that arise during evaluation for surgical intervention to resect the epileptogenic zone.

Four pediatric clinical cases will be presented which illustrate particular advantages of MEG in pediatric epilepsy. These children range in age from 6 months to 15 years and had MEG performed as a component of their pre-surgical evaluation for medically intractable epilepsy. Some of the points demonstrated will include: 1) unique usefulness of ictal MEG in pediatric patients; 2) role of MEG when EEG interictal or ictal data is non-localizing; 3) role of MEG in non-lesional or multi-lesional MRI cases; 4) role of MEG in surgical planning.

IDENTIFYING THE EPILEPTOGENIC ZONE WITH MEG: MYTHS AND REALITIES

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When video-EEG monitoring is unable to pinpoint the epileptogenic zone, or when the results are not entirely concordant with other structural and functional tests, another method for recording and localizing neural signals, magnetoencephalography (MEG) may clarify the origin of the epileptic discharges. The results of electroencephalography can be especially confusing when the patient has undergone a previous neurosurgical procedure, whereas MEG is not influenced by alterations or abnormalities of the skull

or alterations of the parenchymal anatomy. In patients with epilepsy, MEG can be used not only to 1) provide more precise localizing information about the epileptogenic zone, but MEG can also 2) explain or enhance the results from other modalities, 3) guide further evaluation (e.g. placement of invasive electrodes), 4) suggest that a patient with apparently generalized epilepsy actually has a focus that should be further investigated for possible resection, or 5) uncover or confirm additional foci thereby eliminating the patient from consideration as a possible surgical candidate.

Because of its complementary role in the workup of patients with epilepsy, MEG has had a high impact on treatment decisions in many cases. Although MEG may not be able to replace invasive EEG recordings, its use may guide the placement and tailor the design of intracranial investigations, and in some patients obviate unnecessary invasive evaluations. Clinical magnetoencephalography has advanced tremendously in the last decade as results from research laboratories have been translated into effective clinical tools. Some myths regarding difficulties and limitations of MEG persist, despite the fact that many obstacles have been overcome. This presentation will address some of the common misconceptions about MEG, and will discuss what the referring physician can expect from a MEG scan.

THE COMING OF AGE OF MAGNETOENCEPHALOGRAPHY

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We already forgot a celebration of the 40th anniversary of the first SQUID recording, and thousands of patients worldwide benefited from MEG's delivery of non-redundant localizing information in an evaluation for epilepsy surgery. Thousands of lives have been changed drastically by the contribution of this very technology. Yet, some still tend to call it a new technology, while some don't even recognize its confirmed invaluable role even in clinical epileptology. Furthermore, new benefits from magnetic source imaging (MSI) are emerging slowly, and efforts on establishing new clinical indications are accelerating. Meantime, some very active national societies such as American Clinical MEG Society (ACMEGS) took the lead on publishing world's first clinical practice guidelines (CPGs), and nurturing educational initiatives from annual courses to year-long clinical fellowships. Thus, it seems that a clear identity of clinical MEG emerged in daily clinical practice after years of confusion. The appropriately educated MEG practitioners and ordering clinicians have all the right reasons to turn a new page, and start asking "MEG - where else", instead of "MEG - what for". This impending leap to the next level, however, requires that we all join forces internationally and speak with one voice. The International Federation of Clinical Neurophysiology (IFCN) society may represent an appropriate logistical framework that we should approach united. If the ISACM aspires to live up its proclaimed role, it should not miss a unique opportunity to facilitate this process. This should not dampen the momentum from any specific priorities of national or international societies.

S3: GETTING A GRIP ON MEG GAMMA-BAND OSCILLATIONS: NEW INSIGHTS FROM MULTIMODAL STUDIES

CHAIRS:

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Numerous magnetoencephalography (MEG) studies have demonstrated that gamma-band oscillations are detectable in various brain regions and modulated by a wide range of sensory, motor and higher-order cognitive tasks. However, the mechanism by which gamma-range activity arises in the MEG signal, the reliability of its detection in MEG and its links to other measures of brain activity are all poorly understood. This symposium addresses these exciting questions by overviewing some of the most recent multimodal studies targeting gamma-band oscillations: Each talk will address the link between MEG gamma activity and its putative correlate in another imaging or electrophysiological technique: MEG vs. fMRI (Talk 1), MEG vs. MRS (Talk 2), MEG vs. PET (Talk 3), MEG vs. simultaneously recorded EEG/ECoG (Talk 4) and MEG vs. simultaneously recorded intracerebral EEG (Talk 5). The talks will explore the state-of-the-art of MEG gamma oscillations by describing how they relate to the BOLD signal and to GABAergic inhibition, and by assessing the reliability of their non-invasive detection. The speakers will also address the specificity of gamma, if any, compared to lower frequency oscillations and discussions will aim to put the multimodal pieces of the gamma puzzle back together and outline paths for future research.

IS THERE A RELATIONSHIP BETWEEN MEG GAMMA ACTIVITY AND THE FMRI BOLD SIGNAL?

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The gamma band activity (GBA) observed in MEG data, especially after inverse modeling, is arguably more robust than that from EEG. However, its relatively low SNR makes non-invasive detection generally more difficult than with invasive methods. Intracranial recordings have reported a positive correlation between GBA and the BOLD response (Logothetis et al., 2001; Mukamel et al., 2005). The increased spatial specificity and similarities in activation pattern of fMRI relative to MEG GBA (e.g. Brookes et al., 2005) have encouraged further comparison; a growing body of evidence confirms the positive correlation between MEG gamma and BOLD (e.g. Zumer et al, 2010). In addition, gamma provides information to predict BOLD independent from, and in some cases better than, other frequency bands (Scheeringa et al., 2011; Magri et al., 2012). We further explore the relation between fMRI and MEG gamma, in contrast to other aspects of neural activity, and extend previous results by identifying distinctions between transient and sustained GBA. Finally, the link between MEG gamma and BOLD is still a matter of debate (Muthukumaraswamy and Singh, 2008) and other open questions include whether they relate in the absence of stimulation and whether fMRI networks can inform on gamma band connectivity.

MEG, MRS, DRUGS AND DYNAMIC CAUSAL MODELING - STUDIES OF GAMMA OSCILLATORY DYNAMICS AND THEIR RELATIONSHIP TO SYNAPTIC EXCITATION/INHIBITION

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In recent years there has been much interest in the use of non-invasive MEG/EEG gamma oscillatory biomarkers as indices of individual variability in health and disease. One of the main reasons for this focus has been the belief that parameters such as gamma amplitude and frequency are intimately related to synaptic properties, such as the balance between excitation and inhibition. In support of this, a limited number of studies have shown a relationship between these oscillatory parameters and baseline concentrations of neurotransmitters such as GABA, although new data suggests that this relationship may be much weaker than previously demonstrated and pharmacological studies have also had mixed results. At the same time, using neurophysiologically informed models of local cortical gamma dynamics offers a potentially more sensitive and informative way of analysing such data. In this talk I will review the current 'state-of-the-art' in combining MEG, MRS, pharmacological manipulation and modelling, in order to try and better understand what drives individual variability in the dynamics of gamma oscillations.

ARE GAMMA OSCILLATIONS RELATED TO RESTING GABA-A RECEPTOR DENSITY? COMBINING INSIGHTS FROM MEG AND FLUMAZENIL-PET

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The mechanisms by which gamma-band oscillations are generated remain poorly understood. Results from experimental and computational neuroscience point to a key role of GABA-mediated inhibition (Bartos et al. 2007; Buzsaki & Wang, 2012; Gouwens et al. 2010). Interestingly, recent studies combining MEG with magnetic resonance spectroscopy (MRS) GABA-concentration measures suggest that the dominant frequency of cortical gamma-oscillations is correlated with the concentration of GABA at rest (Muthukumaraswamy et al., 2009; Gaetz et al., 2011). We report findings from a recent multimodal study in which we investigated the relationship between gamma oscillations and GABA-A receptor density, determined respectively from MEG and positron emission tomography ([11C] Flumazenil-PET) data. While the flumazenil uptake recordings were conducted during rest, the MEG data were collected during a visual working memory task. We found memory-load dependent task-induced increases in gamma-band (60-90 Hz) power across a widely distributed network. Interestingly, in the occipital cortex, the PET-flumazenil measures correlated negatively with the peak gamma frequency and positively with gamma-band amplitude. These results extend previous MEG-MRS findings by providing the first link between GABA-A receptor density and task-related gamma oscillations and allow us to fine-tune our understanding of the link between GABAergic inhibition and gamma-band oscillations.

COMPARING MEG, EEG AND ECOG RECORDINGS OF HIGH-FREQUENCY ACTIVITY

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Gamma-band activity seems to be an important signature of local cortical information processing. While these signals are often readily discernible in intracranial recordings, their detection in MEG and scalp EEG measurements can be challenging. To investigate the visibility of gamma-band signals in non-invasive recordings, we have conducted simulations in realistic geometries and with different kinds of MEG sensor arrays as well as compared the signals in simultaneously performed electrocorticographic (ECoG) and MEG recordings in epileptic patients by looking at the correlation and coherence between these two sets of signals. In addition, we have developed signal-processing methods to reduce intrinsic noise in MEG recordings and thus to boost the detection of the weak gamma-band signals, up to enabling visualization of single-trial gamma responses in the early visual cortices. We have also compared the signal-to-noise ratios in MEG and scalp EEG for these visual gamma responses.

GAMMA GAMMA HEY – WHEN AND WHERE DOES HIGH-FREQUENCY MEG ACTIVITY CORRESPOND WITH INTRACRANIAL EEG FINDINGS?

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Intracranial EEG (icEEG) recordings in neurosurgery patients are a powerful electrophysiological tool for the investigation of high-frequency activity in humans. High-frequency activity, including the gamma band, can be reliably observed with icEEG. With the emerging role of MEG in noninvasive investigation of gamma band activity, knowledge from icEEG can inform MEG researchers under which conditions gamma band activity can be recovered from noninvasive recordings. Our group and others have now been able to successfully acquire MEG simultaneously with intracranial EEG, and several studies exist with MEG and intracranial EEG acquired in separate recording sessions. These powerful datasets allow us to gain some insight into the strength and spatial extent of gamma band activity needed in order to be feasibly measurable with MEG. Additionally, the accuracy of MEG forward models are another limiting factor into whether weak signals can be reliably reconstructed, and intracranial EEG can provide us further insight on this aspect as well. We shall present the latest results from our ongoing simultaneous recording effort with a spatial navigation task, and discuss the findings in the context of gamma band results from our previous study involving a reading task as well as recent reports from other groups.

ISACM S2: EMERGING CLINICAL INDICATIONS

CHAIR:

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THE MAGIC-AD PROJECT: TOWARDS AN MEG BIOMARKER IN DEMENTIA

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Alzheimer's Disease is the most frequent form of dementia and its neuropathology causes loss of neurons and synapses as well as accumulation of the beta amyloid protein and phosphorilation of the Tau protein. All these lead to an impairment of the brain regions to communicate to each other and thus causing a disconnection syndrome. Our group has been trying to demonstrate how Magnetoencephalography (MEG) could evaluate the early impairment in the functional networks by using the metrics of functional connectivity in both the sensor and the source space. In this talk we will indicate the profiles of network disruption in patients with Mild Cognitive Impairment (MCI). Then we will describe how the hypersynchronization of the functional networks could be a good biomarker for predicting who of the MCI patients will develop or not dementia. These profiles have been compared with data from functional connectivity or other biomarkers such as the phosphorilation of the Tau protein, the accumulation of the beta amyloid or with data from healthy elders taking scopolamine. Finally, we will go through the description of an international study, the MAGIC-AD project, in which seven different MEG labs were involved. This was a blind study trying to evaluate whether fcMEG profiles could achieve a high classification, at the individual level, between MCI and controls. The accuracy of correct classification was higher of 80% which is high percentage for a blind study. We will discuss all these findings based on ideas of the neuropathology of the disease.

CORTICO-BASAL GANGLIA OSCILLATORY CONNECTIVITY AND THE PATHOPHYSIOLOGY OF PARKINSON'S DISEASE: INSIGHTS FROM SIMULTANEOUS MEG AND DEEP BRAIN RECORDINGS IN PARKINSONIAN PATIENTS

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Parkinson's disease (PD) is common debilitating neurological disorder afflicting movement and cognitive processing. Recent theories of its pathophysiology have highlighted a potential pathological role for excessive oscillatory synchrony within cortico-basal ganglia networks. Here I present insights and also discuss the challenges of an approach combining simultaneous MEG and deep brain recordings in PD patients following surgery for the insertion of deep brain stimulation electrodes. These studies have revealed the presence of multiple cortico-basal ganglia networks that are distinct in their patterns of activation, their cortical topographies and in their preferred frequencies of interaction. Moreover the relevance of these networks to parkinsonian symptoms is exemplified by medication (levodopamine) related changes in coupling correlating with clinical motor improvement. Finally, I will discuss future avenues for this work within the framework of describing specific parkinsonian clinical impairments in terms of stereotyped oscillatory network abnormalities.

FROM BABYSQUID TO BABYMEG: RECENT ADVANCES IN CLINICAL PEDIATRIC MAGNETOENCEPHALOGRAPHY

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Recent technological advances in pediatric MEG present new opportunities for pediatric hospitals facing the challenge to offer high quality clinical services to their patients. Child-size MEG dewars promise higher spatial resolution and sensitivity compared to the conventional adult systems, from which both clinical and basic research can benefit. Here, we present preliminary findings of three studies from our pediatric MEG facility equipped with the BabySQUID system. High-density MEG and EEG data were recorded from three epilepsy children with tuberous sclerosis complex. Interictal spike generators were localized with ECD and wMNE. Granger causality at the source level identified the underlying epileptogenic network and the propagation of interictal activity. In all patients, the epileptiform activity derived from abnormally developed tissue surrounding prominent tubers and propagated to the surrounding tissue of neighbor tubers. Our findings revealed a complex epileptogenic network that was hidden from the standard clinical MEG/EEG analysis. The functional and anatomical abnormalities in the sensorimotor network of children with hemiplegic cerebral palsy (HCP) were examined in a separate study. Somatosensory evoked fields were recorded from six HCP and six aged-matched typically-developing (TD) children. An altered somatotopic organization was observed in the affected hemisphere of 5 HCP suggesting an abnormal somatosensory processing mechanism in the sensorimotor network of HCP. In our third study, three children with autism spectrum disorder (ASD) and four TD children completed an auditory lexical decision task. M100 auditory evoked responses identified in the ASD group were delayed (by ~10ms) in both hemispheres compared to TD. Time frequency analysis showed decreased activity in the early auditory-evoked gamma oscillation in ASD for both hemispheres. Our findings suggest a possible atypical processing of auditory word meaning in ASD. Finally we will present updates regarding the prototype 384-sensors BabyMEG system arriving at BCH, which is especially designed for neonates, babies, and toddlers.

MEG AND MILD TRAUMATIC BRAIN INJURY/CONCUSSIONS

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Traumatic brain injury (TBI) is a leading cause of sustained impairment in military and civilian populations. However, mild TBI (mTBI)/concussions are very difficult to diagnose using conventional MRI or CT. Injured brain tissues in mTBI patients generate abnormal slow-waves (1-4 Hz) that can be measured and localized by resting-state magnetoencephalography (MEG). In this study, we develop a voxel-based whole-brain MEG slow-wave

imaging approach for detecting abnormality in patients with mTBI on a single-subject basis. A normative database of resting-state MEG source magnitude images (1-4 Hz) from 79 healthy control subjects was established for all brain voxels. The high-resolution MEG source magnitude images were obtained by our recent Fast-VESTAL method. In 84 mTBI patients with persistent post-concussive symptoms (36 from blasts, and 48 from non-blast causes), our method yielded positive detection rates of 84.5%, 86.1%, and 83.3% for the combined (blast-induced plus non-blast), blast, and non-blast mTBI groups, respectively; with no false positives in the normal controls. We found that prefrontal, posterior parietal, inferior temporal, hippocampus, and cerebellar areas were particularly vulnerable to head trauma. The results also showed that MEG slow-wave generation in prefrontal areas positively correlated with personality change, trouble concentrating, affective lability, and depression symptoms. The neuronal mechanism of MEG slow-wave generation is due to de-afferentation caused by axonal injury and/or blockages/limitations of cholinergic transmission in TBI. This study shows that MEG slow-wave source imaging effectively localizes injured areas, and supports MEG as a tool to assist in the diagnosis of mTBI.

MEG AND STROKE RECOVERY

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Stroke alters cortical inhibition in both hemispheres. Although disinhibition of the affected hemisphere may be necessary for plastic reorganization, hyperexcitation of the healthy hemisphere may hinder recovery. Thus understanding of inhibitory changes and their relationship with recovery is critical in developing novel methods for stroke rehabilitation. Tactile and proprioceptive input coordinates and recalibrates motor cortex activity by regulating its excitability. Accordingly, afferent somatosensory input has been shown to modulate the motor cortex oscillations, leading to an initial suppression followed by a rebound of the rhythm. The suppression is suggested to reflect an activated state of motor cortex whereas rebound of the 20 Hz oscillations is considered to reflect increased inhibition or deactivation of the motor cortex.

We examined ~20-Hz oscillatory brain activity during tactile stimulation and passive movement of the index fingers in 22 healthy subjects and acute stroke patients with whole-scalp magnetoencephalography (MEG) to compare the effect of the two different somatosensory stimulus types on motor cortex oscillations and to monitor alterations in motor-cortex excitability after stroke.

In healthy subjects, the rebound was stronger to passive movement than to tactile stimulation indicating strong influence of proprioception on motor-cortex excitability. In contrast, the suppression amplitudes did not differ between the two stimulus types, suggesting that suppression and rebound represent activity of two functionally distinct neuronal populations. In stroke patients, alterations of the rebound of ~20-Hz oscillations correlated with functional recovery. The results indicated that lesion site and size have substantial effect on alterations of cortical excitability both in the affected and in the healthy hemispheres. ~20-Hz rhythm modulation to passive movement could be a useful tool to observe stroke-induced alterations in motor cortex inhibition and to evaluate the effect of novel rehabilitation approaches on motor cortex excitability.

S4: NONLINEAR AND TRANSIENT DESCRIPTIONS OF BRAIN ACTIVITY

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MEG signals have often been described using linear measures such as amplitude, power, frequency, and phase; and based on narrow-band interactions between brain areas. In fixed brain states (e.g. at rest) these descriptions also tend to be time averaged. Such approaches have been successful in revealing task-dependent oscillatory activity and MEG 'resting state' interactions. This symposium will focus on significant advances to these linear and static approaches. First, it is known that the brain is inherently non-linear and its signals are chaotic. Such signals are characterized by parameters such as entropy (complexity), and pairwise measures such as mutual information and transfer entropy. Since narrow-band signals have low complexity, non-linear measures are generally applied to broad-band signals. We examine informational dynamics by looking at event-related changes in complexity and pairwise measures of shared information as indicators of functional network connections. Second, we expect the brain to be able to reorganize and coordinate on very fast time-scales and so a static, time averaged description, e.g. of the resting state, is inadequate. Here, we highlight approaches that provide transient, time-varying information about neuronal interactions in the brain. It will be shown that these complementary methods lend new insight into the spatiotemporal structure of brain activity.

NEURAL INFORMATION DYNAMICS AS SEEN BY MEG

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Information theoretic measures can quantify key elements of distributed computation in neural systems, such as the storage, transfer, and modification of information. This way, they help to better understand the computational algorithm implemented in a neural system. This understanding cannot be reached by detailed biophysical modeling alone. In other words, we may biophysically well understand why brain signals look the way they do, but still not understand what these signals are worth in terms of information processing proper, as will be shown in a simple toy model. The missing link between neural dynamics that can be modeled at the biophysical level and the computational algorithms implemented by these dynamics can be provided by information theoretic methods. Two such methods, transfer entropy and local active information storage will be demonstrated in two examples. In example one, a time resolved analysis of information transfer between MEG sources in various perceptual closure tasks is used to

test psychological theories about the algorithm our brains use to perceive objects when sensory information is incomplete or ambiguous. In example two, we show that information storage is reduced in patients suffering from autism spectrum disorder.

DYNAMIC CENTRALITY AS A MECHANISM OF CROSS-NETWORK COUPLING

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Previous work reported evidence of the Default Mode Network as a central core of cross-network coupling. In this talk, we extend these results by adopting a graph based analysis to investigate the dynamics of cross-coupling properties of six resting state networks: Dorsal and Ventral Attention, Default Mode, Language, Motor and Visual Networks. Two important aspects of brain interactions at rest are discussed: the evidence of transient hubs allowing a dynamic cross-network coupling and its relationship with the global efficiency and modularity of the brain. In particular, three networks, namely the Default Mode, Dorsal Attention and Motor behave as dynamical, i.e. acting at distinct times, connectivity hubs of the brain. Interestingly this model seems to be driven by an overall optimization criterion responding to the global efficiency and modularity of the brain as a system. These results taken together pave the way to interesting new models of information flow in the brain.

THE DISORDERED BRAIN: MEASURING NEURAL NETWORK COMPLEXITY IN SCHIZOPHRENIA AND NEURODEVELOPMENT

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In recent years, measurement of signal entropy has been highlighted as a new means to provide novel information about non-linear neural network dynamics in health and disease. In this talk, I will discuss our recent work in this area. I will begin by discussing entropy measurements in brain areas rendered active by cognitive tasks, and I will show that an increase in local neural processing generates localised and transient increases in complexity in the MEG signal. Following this, I will explore the relationship between entropy and more established time-frequency decomposition methods, which elucidate the temporal evolution of neural oscillations. I will show evidence for a direct but complex relationship between entropy and oscillatory amplitude, which suggests that these independent metrics are complementary. Finally, I will show two emerging applications of signal entropy measurements: Firstly, I will use entropic transformation it to shed light on aberrant neurophysiological processing in schizophrenia, including how these metrics are in agreement with a disconnection hypothesis. Secondly, I will show evidence for changing entropy in well-known large scale networks, throughout neurodevelopment.

FAST TRANSIENT NETWORKS IN SPONTANEOUS BRAIN ACTIVITY

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It has recently been shown that functional connectivity within large-scale networks of spontaneous activity exhibits temporal variability on a time scale of seconds to tens of seconds. However, to provide an effective substrate for cognitive processes, functional brain networks should be able to reorganize and coordinate on a sub-second temporal scale. We present a novel approach to characterise whole brain functional connectivity dynamics at high temporal resolution. The method is underpinned by a hidden Markov model (HMM), which infers the points in time at which different states occur, providing an intelligent pooling over short-lived transient synchronisation events. By applying this method to source projected MEG recordings of resting state activity, we identified wideband (4-30 Hz) transient (100-200 ms) brain states with spatial topographies similar to those of well-known resting state networks. By assessing temporal changes in the occurrence of these states, we demonstrate that within-network functional connectivity is underpinned by coordinated neuronal dynamics that fluctuate much more rapidly than has previously been shown. We further assessed cross-network interactions by studying the relationship between the inferred states and show that anticorrelation between the default mode and dorsal attention networks is consistent with an inability of the brain to transition directly between these transient states.

BEREITSCHAFTSKOMPLEXITÄT: GOING BEYOND THE APPARENT

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Since the discovery of brain oscillatory activity, the ability to decode information from brain oscillations promised a better understanding of the basic principles of brain function. However, partly due to limited computational capacities, most established measures of task-free and task-related brain activity are based on averaged amplitude or source power, while the electric or magnetic signals recorded at the millisecond-to-millisecond range exhibit chaotic and highly complex features related to dynamic state transitions not reflected in these measures. These state transitions, however, can be characterized by entropy measures, e.g. rank vector entropy (RVE), a non-parametric partial symbolic analogue to metric entropy that ignores the absolute signal amplitude. We found that the same state change resulting in a slow negative potential shift preceding voluntary movements by up to 2 seconds (<0.1Hz) as Bereitschaftsfield (BF) can be detected by applying the RVE algorithm to broadband beamformer- processed magnetoencephalographic (MEG) data above 4 Hz. Due to the similarity to the BF, we refer to the RVE waveform associated with voluntary self-paced movements as Bereitschaftskomplexität. Our findings indicate that RVE may be a powerful tool to investigate causal links between dynamic brain states and human behavior that were previously inaccessible.

EEG SOURCE IMAGING OF BRAIN RESTING MICROSTATES

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In the brain there are different generators working independently in the same frequency, as indicated by the fact that different scalp potential maps exist for any given frequency with different time-courses. On the other hand, different brain areas can be active in different frequencies but with similar time courses. The global scalp potential map represents the global momentary state of the brain defined by the sum of all momentary active sources independent of the frequency with which each source is active. Surprisingly, only a few distinct map configurations (topographies) dominate the spontaneous EEG and these configurations remain stable for a certain variable time period of around 100 msec. Transitions from one to another map configuration are very rapid (few msec). This observation led to the concept of functional microstates of the brain as the building blocks of mentation (Dietrich Lehmann, 1972). The temporal sequence of the microstates are thought to reflect the continuous stream of thoughts. We will illustrate the concept of functional microstate and we will show how, on a large dataset (>50), the salient topographies can be used as spatial filters to estimate the underlying sources of the resting state networks.

METASTABILITY AND COLLECTIVE FREQUENCIES IN OSCILLATORY BRAIN NETWORKS

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MEG studies of spontaneous activity reveal that some brain areas recurrently display the simultaneous emergence and dissipation of oscillations in a limited frequency range. These intermittent collective oscillations lead to correlated amplitude fluctuations of band-limited signals. However, the biophysical mechanism at the genesis of these collective oscillations remains unclear. We present a novel mechanistic scenario to explain these experimental observations (Cabral et al., 2013). Using a computational model, we show how a system of coupled oscillators (with realistic whole-brain connectivity and conduction delays) may display metastable partially-synchronized states (or chimera states). Due to delays, the synchronized units oscillate at reduced collective frequencies. This mechanism originates slow and structured amplitude envelopes of band-limited signals, fairly reproducing MEG data from 10 healthy subjects at rest. The results show that the large-scale neuroanatomical connectivity provides an optimal network structure to support a robust metastable regime in which band-limited collective oscillations emerge transiently. This mechanism may be at the origin of the correlated envelope fluctuations observed in resting-state MEG data.

A TASK-INDEPENDENT NETWORK REVEALED BY SYMBOLIC MUTUAL INFORMATION

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Symbolic mutual information (SMI) is a pair-wise measure of shared information between two time series. It is non-parametric and is independent of signal amplitude. This measure may be applied to voxel time series such as from MEG data transformed by a beamformer, resulting in a matrix of functional connection strengths (i.e., the amount of shared information). The SMI matrix can be displayed as a collection of 3D images – one image per seed voxel. SMI was applied to working memory (n-back test) data and to task-free resting MEG data in the same subjects. The functional networks show the strongest connections along the ventral midline structures. These networks are not strongly modulated by task difficulty and are extremely robust. Individual subject differences are worth noting, with schizophrenics showing much greater connectivity than control subjects. Both methods and the results of preliminary studies will be shown.

ISACM S3: ADVANCES IN MULTI-MODAL INTEGRATION

CHAIR:

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MULTIMODAL IMAGING IN THE OPERATING THEATER: THE HOUSTON EXPERIENCE

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The purpose of epilepsy surgery is to convert medically intractable epilepsy into medically tractable epilepsy. Successful surgery requires two key elements. The first is identification of the seizure-onset zone and critical projected network, and the second is identification of eloquent cortex (critical nodes of distributed network function in or near the resection target). Individual imaging and functional modalities including MRI (fMRI, DTI and cortical thickness maps), EEG, iEEG, MEG, PET, SPECT, and CT each may offer a significant contribution to these goals. Particularly for cases involving the use of stereo-EEG, combining these modalities may result in increased confidence in a particular interpretation of the clinical data, or demonstrate disparities that require resolution either through reasoning, additional information from other test modalities or expansion of the possible hypotheses. In some cases, multimodal integration results in the conclusion that no resective surgery is reasonable, entirely changing the plan of treatment. This talk will review the real-world application and impact of multi-modal imaging, both prior to and in the operating suite, via a series of case presentations.

PUTTING THE "BIO" INTO BIOMARKER

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Biomarkers for neuropsychiatric disorders, such as autism spectrum disorders (ASD), can play several important roles: diagnostic, prognostic, stratification and as indices of treatment response. As a neurophysiologic brain activity sensor, MEG has a clear opportunity to contribute, spatially, temporally and spectrotemporally, to the identification of such markers. But are they "bio"markers?

In order to justify the moniker, "biomarker", it is evident that at least a 'biologically-plausible mechanism' should be implicated. To that end, much

recent work has focused on invoking multiple non-MEG modalities to support the biological interpretation of emerging MEG signatures: in short, putting the "bio" into biomarkers.

Several large cohorts of school-aged children with diagnoses on the autism spectrum, as well as typically-developing controls, have undergone MEG studies focused primarily on auditory processing, using simple tone stimuli and mismatch paradigms. In addition to MEG, these children underwent MRI at 3T with sequences including diffusion tensor imaging, high angular resolution diffusion imaging and spectrally-edited MR spectroscopy, optimized for the detection of GABA and glutamate.

Key MEG findings that have emerged include delayed M50 and M100 response latency in ASD. This has been associated with atypical development of the white matter projection fibers linking thalamus to auditory cortex, as revealed by quantitative diffusion imaging. A "bio"physics hypothesis of abnormal central conduction velocity emerges, as a model of multi-modality converging evidence supporting the "bio" claim, intrinsic to "biomarker". Similarly, atypically-low gamma-band phase synchrony is evident in ASD. Yet, the claim of "bio"marker is weak until coupled to evidence for an imbalance of excitatory and inhibitory neurotransmitters, revealed by MR spectroscopy.

Converging evidence from alternative modalities can augment the interpretation of MEG signatures of neuropsychiatric conditions, adding support to the claim that these potentially represent not just "markers", but "biomarkers".

INTEGRATING MULTIPLE IMAGING MODALITIES OF SPONTANEOUS BRAIN ACTIVITY

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The brain spontaneously produces activity patterns at rest and sleep. These intrinsic events cascade through brain systems in waves that track anatomy and functional networks. Hence, it may be possible to use these events to unravel the underlying structure of brain systems, both in healthy and diseased brains. The signals produced from the brain's spontaneous activity can be measured non-invasively, which depends upon the desired signal measurement: magnetic (MEG), electrical (EEG), metabolic (FDG-PET), or hemodynamically (fMRI or NIRS). We can also measure structural connections of white matter tracts with diffusion MRI. The human connectome is the sum of all the structural and functional connections that the spontaneous activity tracks. It has been demonstrated by various groups that the measurement of these events can be used to characterize brain organization and the locus of dysfunction, rapidly, and in individual patients. By combining the information from resting-state MEG and from a short resting-state fMRI imaging sequence, lasting about 10 minutes, one can map brain function (and dysfunction) for treatment planning in diseases such as epilepsy and brain tumors.

OSCILLATIONS AND BRAIN STRUCTURE IN PSYCHIATRY

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Background: Structural and functional methods are advancing to the point where very specific brain abnormalities are identified in psychiatric disorders. Combining structural and functioning findings will likely have a synergistic effect, fostering development of more detailed hypotheses regarding brain pathology than is possible examining MEG or structural data in isolation.

Methods: MEG and structural MRI data were obtained in studies examining associations between (1) auditory encoding processes and gray matter in schizophrenia (SZ), and (2) resting-state alpha activity and thalamic volume in autism spectrum disorder (ASD).

Results: (1) Left superior temporal gyrus low-frequency and 40 Hz steady-state gamma abnormalities distinguish SZ and healthy controls. Relationships between superior temporal gyrus gray matter and 40 Hz steady-state gamma activity observed only in the adult controls suggest that damage to STG gray matter in SZ disrupts left STG 40 Hz gamma (but not low-frequency) activity. (2) Children with ASD have abnormally increased resting-state alpha activity. Relationships between thalamic volume and resting-state Calcarine alpha power observed only in the typically developing control group suggest thalamocortical pathology in ASD.

Conclusions: With a move in the field to identify neural measures (i.e., neural endophenotypes) as targets for treatment, multimodal studies will help define the types of treatments likely to be effective. As an example, clinical trials seeking to normalize superior temporal gyrus auditory gamma rhythms in SZ will need to take into account the gray matter structural damage that likely occurs prior to the onset of the disease. Considering the NIMN RDoC framework, multimodal studies are needed to determine whether neural endophenotypes that appear common to different DSM disorders (e.g., gamma abnormalities in SZ, and ASD, and ADHD) are the same or instead arise due to different mechanisms.

RESTING-STATE AND TASK-INDUCED OSCILLATORY BIOMARKERS IN HEALTH AND DISEASE: THEIR USE, RELATIONSHIP TO MR MEASURES, AND NEUROPHYSIOLOGICALLY INFORMED MODELLING

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It is becoming increasing clear that sensory/motor oscillatory responses, such as visual and motor gamma, may provide a new direct window onto synaptic function, providing translational biomarkers of healthy individual variability, disease state and pharmacological manipulation. At the same time, new approaches to MEG analysis have allowed the use of resting-state paradigms that reveal oscillatory networks that match those found with BOLD-fMRI, and hence may also provide a richer and more direct measure of disease-related impairments in functional connectivity. Using examples from healthy control data, pharmacological studies, epilepsy and Alzheimer's cohorts, this talk will illustrate the use of these measures and

how modelling frameworks such as DCM can be used to provide neurophysiologically relevant information that goes beyond, and is more sensitive than, the simple data features.

S5: OPTICALLY-PUMPED MAGNETOMETERS FOR MEG

CHAIRS:

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Optically-pumped, or atomic, magnetometers have made significant progress in the last years, specifically for the application of magnetoencephalography (MEG). From measuring evoked responses with few channels, attempts are currently made to localize neural sources with arrays of sensors. The current development is largely driven by the technical advantages to operate without cryogenics and to allow for systems adaptable to different subject populations, particularly children. Furthermore, simulations in realistic geometries show the potential of these uncooled sensors for MEG and aid their future development. At the same time, the proximity of these sensors to the cortex could enable recording of signals previously inaccessible by MEG.

CHIP-SCALE OPTICALLY-PUMPED MAGNETOMETERS FOR MEG

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Optically-pumped magnetometers are emerging as an attractive alternative to SQUID magnetometers due to their flexible geometry and uncooled operation. Microfabricated versions of these magnetometers provide a possibility for inexpensive fabrication, small size and weight, and very close proximity between sensitive volume and the surface of the sensor.

Recently, we have built the core components of a 20-channel magnetic imaging system. We have recorded evoked magnetoencephalography signals in several subjects in the seven layer mu–metal Berlin Magnetically Shielded Room 2 . Each sensor was mounted on the tip of a spoke and the spokes were inserted into the holes of a helmet shaped holder. The spokes could be moved radially within the helmet to position the sensors as close as possible to each subjects scalp and to optimize the configuration for the specific measurement. The sensitive volume of 3.5 mm3 could be positioned roughly 5 mm from the scalp. The sensors had the size of less than 1 cm3 and were fiber-coupled to a control unit. The component of the magnetic field normal to the surface of the head was measured. We have made the first steps toward localizing magnetic sources inside the brain with the 20-channel flexible sensor array.

WHAT DO WE GAIN BY MEASURING MEG RIGHT ON THE SCALP?

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The performance of conventional SQUID-based MEG devices is hampered by the large distance from the cortex to the sensors. In contrast with SQUIDs, optical or atomic magnetometers (AM) do not require cryogenic temperatures and therefore extreme thermal insulation is not needed, which allows these sensors to be within millimeters from scalp. The reduced distance to neural sources should translate into higher signal amplitudes and better spatial resolution. I will present our simulations in realistic head and sensor-array geometries to quantify the gain of measuring MEG near the scalp. We have compared the overall signal strengths, lead-field correlations, point spread functions and localization errors of cortical sources when measuring with a conventional SQUID-based array comprising 102 magnetometers and with a hypothetical array of 102 AMs located within millimeters from the scalp. Our results indicate substantial increase in signal amplitude and reduction of the point spread when recording MEG with sensors on the scalp compared to conventional SQUID arrays. Thus, if the intrinsic noise level of AMs approaches that of SQUIDs, AMs may offer other benefits than just cryogen-free operation.

RETRO-REFLECTION BRAIN ATOMIC MAGNETOMETER SYSTEM AND SOURCE LOCALIZATION

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We report a retro-reflection probing design of an brain atomic magnetometer (AM) for magnetoencephalography (MEG), which has a wide measurement area over a human head. In comparison with a superconducting quantum interference device (SQUID)-based MEG system, the AM system has advantages of comparable or higher sensitivity, no need for liquid helium consumption and easy to implement multi-channel recording. Tangential field component recording with a retro-reflection probe scheme enables to localize the MEG source current dipoles. We describe measurements of auditory evoked fields (AEF) from a human brain as well as localization of dipolar phantoms and auditory evoked fields. A clear N100m peak in AEF was observed with a signal-to-noise ratio of higher than 10 after averaging over 250 stimuli. Currently the intrinsic magnetic noise level is 4 fT/Hz1/2 at 10 Hz.

PROGRESS TOWARD A MULTI-CHANNEL MAGNETOENCEPHALOGRAPHY SYSTEM USING OPTICALLY PUMPED ATOMIC MAGNETOMETERS

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We are working to develop a 36-channel array of optically pumped atomic magnetometers (AMs) to perform magnetoencephalography (MEG) with the goal of localizing magnetic sources within the human brain. The 36-channel array will consist of nine 4-channel sensor modules where the channels within each sensor will be spaced by 19 mm and each sensor will cover a 40 mm by 40 mm area of the head. In a previous 4-channel AM prototype, we demonstrated the measurement of evoked responses in both the

auditory and somatosensory cortexes. This prototype had a 5 fT/Hz1/2 sensitivity. In the current version of the AM under development we are maintaining the previous sensitivity while implementing several improvements, including increasing the bandwidth from 20 Hz to more than 100 Hz, reducing the separation of the active volume of the AM from exterior of the sensor from 25 mm to 10 mm or less, and reducing the active sensor volume by a factor >10 to ~15 mm3. We will present results on the performance of our most recent AM prototype and progress toward developing a complete MEG system including a person-sized magnetic shield to provide a low-noise magnetic environment for MEG measurements.

S6: MAGNETIC NANOPARTICLE IMAGING BASED ON AC SUSCEPTIBILITY AND MAGNETORELAXOMETRY MEASUREMENTS

CHAIR:

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Magnetic nanoparticles (MNP) open new pathways in cancer therapy and non-invasive diagnostics. For the development of magnetic thermoablation and magnetic drug targeting, non-invasive imaging methods which provide specific and quantitative images of MNP are of vital importance. Magnetorelaxometry (MRX) and AC susceptibility (ACS) measurements are two techniques which generate specific MNP signals that can be differentiated from tissue background. Recently, various new spatial encoding schemes for MNP imaging based on MRX and ACS have been proposed and experimentally demonstrated. These imaging methods are applicable to a wide range of MNP having various physical properties and allow for detection of MNP that are specifically tailored to their therapeutic applications rather than to their performance as imaging tracers. With a comparably large field of view and moderate excitation fields which avoid unintentional side effects like hyperthermia and neural stimulation, these imaging modalities may complement and support the powerful imaging modality of magnetic particle imaging (MPI), whose performance depends strongly on physical properties of tracers.

This symposium aims at collecting current technical and theoretical developments in the rapidly expanding field of quantitative nanoparticle imaging for therapeutic and diagnostic applications.

CHARACTERIZATION AND LOCALIZATION OF CANCER USING MAGNETIC RELAXOMETRY

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Magnetic Relaxometry methods have been utilized to determine specificity of various biomarkers for multiple cancer types using cell cultures and animal models. Magnetic nanoparticles were developed specifically for this program with very low dispersity and high magnetic moment. These nanoparticles were conjugated to a variety of biomarkers using specialized biochemical techniques and incubation and titration measurements carried out to determine specificity and magnetic moment per cell for targeted cells. Animal models were then used to study in vivo these biomarkers for breast, ovarian, and prostate cancer in conjunction with several major cancer research centers. The results show high efficiency for cancer detection and have been used to determine efficacy of the magnetic Relaxometry method for using an animal model in cancer research. This application takes advantage of the linear relationship between measured magnetic moments of a tumor and the number of cancer cells present and also the ability to directly measure the percentage of injected material reaching the tumor in vivo.

QUANTITATIVE IMAGING OF MAGNETIC NANOPARTICLE DISTRIBUTIONS IN ANIMAL-SIZED PHANTOMS USING MAGNETORELAXOMETRY

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Quantitative knowledge of the spatial distribution of magnetic nanoparticles (MNP) inside a tumour and organs is essential for the success of novel cancer therapy approaches based on magnetic nanoparticles. Magnetorelaxometry (MRX) is a non-invasive method for specific quantification of MNP. In MRX the decay of the net magnetic moment of the MNP distribution following a moderate (~mT) magnetic field pulse is detected by superconducting interference devices (SQUIDs). Employing multiple SQUIDs the spatially resolved magnetic field generated by the magnetized MNP distribution can be recorded. Using multiple inhomogeneous magnetizing fields has been proposed for the task of encoding spatial information into the MRX signal.

Here, we demonstrate this approach experimentally by imaging quantitatively MNP distributions in animal-sized phantoms. We employed up to 128 magnetizing coils for signal generation and our 304-channel SQUID-magnetometer for detection. Animal sized phantoms consisting of gypsum cubes (1cm3) with defined MNP content were used for the evaluation of the MRX imaging performance. We obtained three-dimensional quantitative images with spatial resolution in the cm-range and a sensitivity of microgram iron per voxel. Our results show that quantitative 3D imaging of MNP distributions by MRX can support the development of cancer therapies based on magnetic drug-targeting and magnetic thermoablation.

EXPERIMENTAL RESULTS ON MAGNETORELAXOMETRY IMAGING OF MAGNETIC NANOPARTICLES WITH M-SEQUENCE BASED INHOMOGENEOUS EXCITATION FIELDS

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The distribution of magnetic nanoparticles can be quantitatively determined from multichannel magnetorelaxometry measurements by least squares techniques. The sequential activation of inhomogeneous excitation fields considerably enhances the imaging quality compared to homogeneous magnetization of the particles. While in first studies single coils were consecutively activated, we recently introduced excitation patterns based on

m-sequences. It could be shown in simulation studies that these sequences require considerably less measurements while preserving the condition of the underlying inverse problem.

Here, we present experimental results on the magnetorelaxometry imaging with multi-coil excitation. The measurements were obtained with a setup comprising 30 excitation coils and the 304 channel SQUID system at PTB, Berlin. Involving animal-sized phantoms and gypsum cubes with defined nanoparticle concentrations, two-dimensional and three-dimensional geometrically defined particle distributions could be quantitatively reconstructed. Imaging results obtained with consecutive activation of single coils and multi-coil excitation patterns based on random sequences and m-sequences were compared.

The obtained results indicate that multi-coil excitation patterns allow for a considerable reduction of the number of measurements while achieving a comparable imaging quality. Therewith, the overall measurement time can be considerably reduced. Alternatively, magnetization and measurement times can be enlarged enabling lower detection limits within the same total measurement time.

HOW TO ADAPT MAGNETORELAXOMETRY ACTIVATION SETUPS FOR QUANTITATIVE MAGNETIC NANOPARTICLE RECONSTRUCTING UNDER REALISTIC NOISE CONDITIONS?

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Magnetic nanoparticles (MNP) are increasingly applied in biomedical modalities due to their interesting properties such as high saturation magnetization and small size. These modalities require an accurate knowledge of the spatial MNP distribution in order to operate efficiently. Magnetorelaxometry (MRX) has a high potential to recover the MNP distribution quantitatively. In this study a MRX setup, consisting of spatially distributed coils, for imaging of rat- and rabbit-sized objects at the Physikalisch-Technische Bundesanstalt (PTB) in Berlin is numerically optimized for accurate MNP reconstructions. Furthermore, we demonstrate the importance of properly modeling noise during MRX imaging reconstructions. First the impact of noise on MNP reconstructions with MRX is investigated for the parameterized setup, and then we analyze how this setup needs to be adapted when prior information on the MRX noise is known. This prior information originates from noise measurements performed with the 304-channel SQUID magnetometer at PTB, Berlin. The proposed noise model allows to determine the sensitivity of the MRX setup more accurately compared to other commonly used noise models.

AC SUSCEPTIBILITY IMAGING OF MAGNETIC NANOPARTICLES

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This study demonstrates a method for alternating current (AC) susceptibility imaging (ASI) of magnetic nanoparticles (mNPs) using low cost instrumentation. The ASI method combines multi-frequency AC magnetic susceptibility measurement with tomographic imaging using an array of drive coils, compensation coils and fluxgate magnetometers. The advantage of ASI is that mNPs can be simultaneously characterized and imaged in a biological medium. System calibration was performed by fitting the in-phase and out-of-phase susceptibility measurements of an mNP sample with a hydrodynamic diameter of 100 nm to a Brownian relaxation model ($R2 = 0.96$). Samples of mNPs with core diameters of 10 and 40 nm and a sample of 100 nm hydrodynamic diameter were prepared in 0.5 ml tubes. Three mNP samples were arranged in a randomized array and then scanned using ASI with six frequencies between 425 and 925 Hz. The ASI scans showed the location and quantity of the mNP samples ($R2 = 0.97$). Biological compatibility of the ASI method was demonstrated by scanning mNPs that were injected into a pork sausage. The mNP response in the biological medium was found to correlate with a calibration sample ($R2 = 0.97$, $p < 0.001$). These results demonstrate the concept and advantages of ASI.

COMBINING SUPERPARAMAGNETIC RELAXOMETRY WITH ULTRA-LOW FIELD MRI FOR EARLY CANCER DETECTION

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Cancer detection at a very early state is important to initiate treatment and/or surgery. One promising sensitive method relies on targeting the cancer cells with antibody labeled single-core magnetic nanoparticles and measuring the relaxation of the magnetization with superconducting quantum interference devices (SQUIDs). However, the localization of the cancerous tissue is impaired by solving an inverse-problem. Conversely, the same magnetic nanoparticles can also provide contrast in magnetic resonance imaging (MRI). By combining superparamagnetic relaxometry and ultra-low field (ULF) MRI, in a single instrument, an improved accuracy of the magnetic moment localization can be achieved and anatomical information is also obtained.

S7: THE MULTIPLE FACETS OF COHERENCE ANALYSIS: FROM NEUROPHYSIOLOGY TO CLINICAL APPLICATIONS

CHAIRS:

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Neurons exhibit rhythmic activity forming the basis for the transient formation of neuronal assemblies. This synchronous rhythmic activity can be measured non-invasively using either electroencephalography (EEG) or magnetoencephalography (MEG).

Interestingly, various sensory and motor processes can entrain this neural rhythmic activity in a specific time-locked and regional manner. One way to reveal these synchronization phenomena is to use the coherence analysis that is an extension of Pearson correlation analysis to the frequency domain, which determines the degree of coupling between two different signals at

a given frequency. In typical experimental design, MEG or EEG signals are compared to other time-locked signals of interest, such as e.g. muscle or vocal activities, or movement kinematics.

In this symposium, four speakers from three different research teams and countries will present the state of the art in using coherence analysis and MEG from pure neurophysiological investigations up to its progressive transfer to clinics for functional mapping or pathophysiological investigations. They will present recent developments and experimental data that shed new light on the neurophysiological mechanisms involved in major human brain functions such as sensori-motor and speech functions both in physiological or pathological conditions.

COHERENCE ANALYSIS WITH MAGNETOENCEPHALOGRAPHY: METHODOLOGICAL CONSIDERATIONS

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The high temporal resolution of MEG affords interesting applications for the analysis of simultaneously acquired peripheral signals. Most studies exploiting this interesting aspect have used peripheral signals recordings aspects of muscle activation (electromyography) or movement (position, velocity). Other examples for useful peripheral signals include continuous auditory input.

A typical analysis approach includes the computation of cerebro-peripheral coherence. This type of analysis allows the investigation of frequency-specific coupling between brain areas and components of the peripheral signal. In this talk, I will review the existing methodological tools that allow the localisation of cerebro-peripheral coherence (including considerations for statistical assessment of results) based on minimum-norm and beamformer algorithms.

In addition, I will present recent developments in this area based on information-theoretic concepts. These concepts represent a generalized framework for the investigation of linear and non-linear dependencies of different types of cortico-pheripheral coupling (including phase-phase and phase-amplitude coupling).

These (and other) recent developments and applications make cerebro-peripheral coupling a relevant tool for investigating the mechanisms underlying the interactions between the human brain and its environment.

EXPLORING COUPLING BETWEEN CORTEX AND MOTOR ACTIONS WITH CORTICOKINEMATIC COHERENCE

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In this talk, I will present recent experimental data investigating the coupling between the kinematics of executed repetitive motor actions and magnetoencephalographic (MEG) signals. This coupling, referred to as "corticokinematic coherence" (CKC; Bourguignon et al. Neuroimage 2011), occurs at movement frequency and its harmonics. A large coherent sensorimotor cortical network is involved in CKC (Bourguignon et al. Neuroimage 2012), with the highest coherence typically located in the primary sensorimotor (SM1) cortex contralateral to the moving limb.

CKC has been successfully computed between MEG and several motor-action-related peripheral signals, such as acceleration, force, pressure, and electromyography (Piitulainen et al. Neuroimage 2013). These findings demonstrate that CKC is closely related to movement rhythmicity. Recent findings showing that both repetitive active and passive finger movements generate strong CKC with similar location in the SM1 cortex (Piitulainen et al. Neuroscience 2013) implicate that CKC is mainly driven by proprioceptive afferent input to the SM1 cortex, with negligible effect of efferent motor commands or cutaneous input.

CKC may be applied to measure and follow the cortical responsiveness to proprioceptive input in health and disease and it also suits for functional mapping of the SM1 cortex in e.g. presurgical evaluation (Bourguignon et al. Brain Topogr 2013).

PROBING ACTION OBSERVATION WITH COHERENCE ANALYSIS

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As highlighted by the preceding talks, corticomuscular (CMC) and corticokinematic (CKC) coherence have provided insights into how brain signals are linked to one's own motor actions. Recent experimental data have shown that these approaches are also relevant to probe the neural representation of others' actions within the action observation network (AON) using ecological action observation paradigms. The AON is a set of segregated brain areas active both during execution and observation of motor actions. As such, it is considered as the human analogue of the frontoparietal mirror-neuron system previously described in the macaque monkey.

In this talk, I will present the different modulations of neural activity identified using CMC and CKC within the observer's brain when viewing others' motor actions (Bourguignon et al. Neuroimage 2013, Hari et al. Phil Trans R Soc B, in press, Marty et al. submitted). Seeing other person's movements phasically modulates the neural activity within a dorsal sensori-motor stream that comprises the primary sensorimotor cortex. These data demonstrate the applicability of the coherence analyses to assess brain encoding of others' actions in a time-sensitive way, thereby complementing functional magnetic resonance studies and opening new perspectives to investigate the AON in humans in an ecological manner.

CORTICOVOCAL COHERENCE: A NEW TOOL TO INVESTIGATE SPEECH NEUROPHYSIOLOGY

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Among the different acoustic cues involved in language comprehension, voice's amplitude fluctuations play a key functional role. Indeed, converging evidences show that ongoing auditory cortex oscillations set their phases to

match speech rhythm. Coherence analysis is therefore a well-suited method to investigate the phasic entrainment of auditory cortex oscillations by the slow fluctuations of the speech signal, i.e., the cortico-vocal coherence (CVC) approach. In this talk, I will first present recent magnetoencephalography data demonstrating significant phase-locking phenomena at the syllabic (4–7 Hz, Peele et al. Cereb Cortex 2012) and sentence (<1 Hz, Bourguignon et al. Hum Brain Mapp 2013) levels at auditory cortices during speech perception. Then, I will show novel evidence of similar coupling during speech production at auditory and sensorimotor cortices (Ruspantini et al. J Neurosci 2012, Bourguignon et al. in preparation). Furthermore, I will show how the auditory cortex phasically tracks the slow amplitude fluctuations of a single speaker's voice in a multitalker background (Vander Ghinst et al. in preparation). Finally, I will show how the CVC approach can provide some hints into the pathophysiology of language impairments in various brain disorders such as autism spectrum disorders (Clumeck et al. submitted), Landau-Kleffner syndrome or central auditory disorders.

S8: 'SLEEPING IN THE MEG'

CHAIRS:

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General theme: Spontaneous brain electrical activity is mostly composed with various types of oscillations at characteristic frequencies, which define rhythms or rhythmic bursts of finite duration, thought to be associated with normal or abnormal physiological functions. During sleep, many of the spontaneous bioelectrical activities, either locally on the cortex or within a large-scale network in the brain, constitute essential neural processes that modify the long-term functionality of the awake brain (e.g. brain plasticity, memory enhancement). Importantly, intrinsic brain activity during sleep also influences neural responses to external stimuli allowing the sleeping brain to be more or less permeable to them. Classically, sleep oscillations are defined using EEG. MEG has several methodological advantages to locate the cortical sources. In this symposium, we will discuss how MEG studies may contribute to a better understanding of basic mechanisms and functions of oscillatory neuronal activity during sleep in normal and pathological populations.

MULTISCALE NEURAL RECORDINGS OF SPINDLES IN HUMAN CORTEX AND SUBCORTICAL STRUCTURES

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One of the most noticeable and earliest described aspects of the human EEG was the waxing and waning bursts of rhythmic ~9-15 Hz activity, lasting ~0.5-3s, that were termed spindles. Marking normal stage 2 sleep, these have been the subject of study since the earliest days of EEG recordings pioneered by Berger and Loomis, and since that era have maintained their central role in sleep research. They have been studied at many levels of investigation, from the biophysical level, where the low threshold calcium currents are implicated in waxing-and-waning 11-15 Hz bursts of action potentials originating in the thalamus that recruit cortical circuits, to the systems level where the electroencephalogram (EEG) and magnetoencephalogram (MEG) measured outside the skull record large scale spatial and temporal coherence in the pattern of spindling across the cortex. In this discussion we will review our findings using combined EEG and MEG studies of spindling activity which show an apparent paradoxical split between wide spread synchrony in the EEG and focal spindling in the MEG. In addition, we will incorporate results from intracranial recordings which help resolve this apparent paradox.

ALTERATION IN SPONTANEOUS OSCILLATORY ACTIVITIES DURING SLEEP ASSOCIATED WITH ENVIRONMENTAL ADAPTATION AND LEARNING

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Our brain is plastic and adaptive in response to environment or stimuli we experience. The neural plasticity occurs not only during wakefulness but also during sleep. Do environmental novelty and learning modulate brain oscillatory activities during sleep? To address this question, we measured spontaneous cortical oscillations by magnetoencephalography together with polysomnography, while human subjects were asleep, and source-localized the origins of oscillations using individual anatomical brain information from magnetic resonance imaging. We found that environmental novelty alters delta oscillation in multiple cortical networks, but in different ways. In the default-mode network, delta oscillation was suppressed, especially in the left hemisphere during slow-wave sleep (SWS). In non-default-mode networks, on the other hand, delta oscillation was also suppressed, but the hemispheric asymmetry was not found. These suggest that environmental novelty may involve hemispheric asymmetry of delta oscillation originating in the default-mode network during SWS. Second, we found that sleep-dependent consolidation of a finger-tapping motor-sequence learning is mediated by spontaneous delta and fast-sigma oscillations originating in the supplementary motor area, especially during slow-wave sleep. Altogether, our recent researches suggest that both environmental adaptation and learning involve modulation of delta and/or sigma oscillations during SWS. (with H. Lin, M. Hämäläinen, T. Watanabe, Y. Sasaki)

GROUPING OF MEG GAMMA OSCILLATIONS BY EEG SLEEP SPINDLES AND SLEEP SLOW OSCILLATIONS

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Sleep spindles and slow oscillations in the human EEG have been shown to be relevant for processing of memories during sleep. Here we investigated whether there is a temporal relation between EEG sleep spindles or slow oscillations and MEG oscillatory activity in the faster frequency bands (>30 Hz) which is considered to reflect local cortical processing of memory representations. MEG and simultaneous EEG were obtained in 12 subjects

during sleep together with standard polysomnography. EEG spindles and slow oscillations were offline detected in the EEG. These events were correlated with power increases in MEG spindle power mainly over prefrontal and occipital cortical areas. During EEG spindles we revealed both transient significant increases and decreases in MEG gamma power, with decreases occurring significantly more often than increases. The modulations in gamma power occurred mainly at sites of increased MEG spindle power, and more often during peaks than troughs within the EEG spindle cycle. Cross-frequency coherence analyses confirmed a strong phase-coupling of gamma band activity with the spindle rhythm. The findings are consistent with the idea that spindles provide a fine-tuned temporal frame for integrated cortical memory processing during sleep.

SLEEP SPINDLES REFLECT COGNITIVE PROCESSING IN NEUROPSYCHIATRIC DISORDERS

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The wide spectrum of sleep disorders in patients with TBI (traumatic brain injuries) occur, hypersomnia, insomnia, and parasomnia (such as acting out dream, nightmares, sleep paralysis , and so on).Sleep-wake regulating centers and associated pathways are damaged in TBI, and these damages will be the cause of disturbances of sleep architecture. Sleep disturbances contribute to fatigue, which may be associated with mental slowness and, slowed information processing. Cognitive dysfunctions may be caused by sleep disturbances and may worsen the impairment in patients who have TBI. We have analyzed sleep spindles of 7 patients following DAI (diffuse axonal injury) using simultaneous EEG and MEG recordings, and showed that spindle alterations of patients' frequency, amplitude, cortical activation source strengths were significantly increased during the postacute to the chronic stage. DAI patients' cognitive functions also improved, with favorable 1-year outcome. Spindle activities may reflect recovery of consciousness, cognitive functions following DAI. In this symposium, I will also discuss spindles as the possibility to reflect consciousness, cognitive processing in other neuropsychiatric disorders such as Epilepsy, Dyslexia, and Schizophrenia. The reduction of sleep-dependent consolidation of procedural memory in Schizophrenia and sleep makes an important contribution to cognitive deficits.

S9: THE 'HOW' AND 'WHY' OF REAL-TIME NEUROIMAGING IN MEG: IMPLEMENTATION AND CLINICAL APPLICATIONS

CHAIR:

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The recent advent of in-line analysis pipelines during MEG data acquisition (i.e., "real-time MEG") has spurred scientists to explore new, hitherto inaccessible, research directions. Real-time MEG provides high-resolution estimates of the temporal dynamics of activity in targeted brain areas in under a second. These signals can then be used to provide neurofeedback to the participant about the quality of their own brain activity or to develop brain-computer interfaces (BCI). Neurofeedback and BCI applications in MEG represent a paradigm shift in how we use MEG technology – moving from brain monitoring to brain therapy. This symposium focuses on the use of real-time neurofeedback in MEG. The panel will present some of the approaches that have been developed for providing source-specific sub-second neurofeedback during MEG scans. Applications of MEG neurofeedback in the basic sciences and in the clinical realms (specifically, tinnitus and stroke) will be presented. Speakers will also discuss the future directions of this burgeoning sub-field of MEG research.

THE 'HOW' AND 'WHY' OF REAL-TIME NEUROIMAGING IN MEG: IMPLEMENTATION AND CLINICAL APPLICATIONS

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- An introduction of the symposium topic
- A non-technical (e.g., flowcharts, pictures) description of real-time MEG
- The implications of real-time MEG for new directions in research
- A brief introduction of the format, panel speakers and topics

REAL-TIME MEG: IMPLEMENTATION AND APPLICATION

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Recent developments in MEG/EEG analysis algorithms and in software packages implementing them as well as the increase of the computational power of low-cost hardware have made real-time MEG easily accessible. Real-time approaches enable not only swift feedback regarding data quality to the experimenter but allow novel paradigms exploiting neurofeedback that lends itself to both basic and clinical neuroscience as well as to brain–computer interfaces. In this talk, I will illustrate how MEG data can be accessed and processed in real time and how the results can be used to modify the stimulus to form a closed-loop system comprising the subject and the measurement and stimulation systems. I will show examples of using selective attention in a neurofeedback setting. I would argue that even though MEG is expensive and non-portable, it may serve well as a rapid development platform for applications that will eventually be translated to EEG.

TARGETED REINFORCEMENT OF NEURAL OSCILLATORY ACTIVITY WITH REAL-TIME NEUROIMAGING FEEDBACK

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Biofeedback and brain-computer interfacing using EEG has been receiving continuous and increasing interest. However, the limited spatial resolution of low-density scalp recordings is a roadblock to the unequivocal monitoring and targeting of neuroanatomical regions and physiological signaling. This latter aspect is pivotal to the actual efficiency of neurofeedback procedures, which are expected to engage the modulation of well-identified components

of neural activity within and between predetermined brain regions. Our group has previously contributed to demonstrate the principles of real-time MEG source imaging. We will show how the technique was further developed to provide healthy subjects with region-specific neurofeedback to modulate successfully predetermined components of their brain activity in targeted brain regions. Overall, our results positively indicate that neurofeedback based on time-resolved MEG imaging has the potential to become an innovative therapeutic approach in neurology and neuropsychiatry.

REAL-TIME NEUROFEEDBACK DURING MENTAL IMAGERY: IMPLICATIONS FOR STROKE RECOVERY

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Mental imagery (MI) is an intervention that has shown promise in its ability to facilitate a higher dose of therapy in patients with neurological injury. During MI, tasks or scenarios are mentally rehearsed in the absence of actual task performance. Of note, script-guided MI can be performed without therapist supervision, reducing health human resource costs associated with therapy. MI however has two primary limitations that reduce its therapeutic efficacy. Reliable methods are needed to inform about a person's capacity to perform MI, and to provide trial-by-trial feedback to improve MI performance. MEG can be used to address these limitations by providing the ideal feedback for improving MI performance: the participant's own brain activity. This session will discuss the current literature related to neurofeedback for MI, present recent findings demonstrating the use of MEG for providing participants information about their own brain activity on a second-by-second basis during real and imagined movement, and lastly highlight the potential role of MEG-based neurofeedback in motor rehabilitation.

NEUROFEEDBACK AS TREATMENT OF CHRONIC TINNITUS: APPROACHES AND PERSPECTIVES

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Tinnitus is a condition that affects approx. 10% of the general population of which again 10% experience a severe impact on their quality of life. Recent research gave rise to the theory that a disturbed excitatory-inhibitory balance originating from, but not limited to, the auditory cortex is an important factor that reveals itself by decreased alpha synchronization in the resting state. Neurofeedback targeted to increase cortical alpha consistently decreases tinnitus distress. Yet, the neurophysiological effects of alpha neurofeedback have remained unclear - both on the level of local synchronization and from the network perspective. Our lab applied neurofeedback training to tinnitus patients, targeting specifically the auditory cortex. Before and after the training, 5 minutes of resting state MEG were recorded and analyzed in source space. Results show that a) Neurofeedback significantly decreases distress in tinnitus patients, b) resting state alpha power is increased focally in the right auditory cortex after training and c) the amount of outgoing connections from a non-overlapping but adjacent region is increased. We conclude that neurofeedback is a surprisingly accurate method to modulate cortical activity and will present how MEG neurofeedback can be implemented using our modular realtime M/EEG framework called ConSole.

S10: COMBINING TRANSCRANIAL CURRENT STIMULATION WITH MEG: PROBLEMS, SOLUTIONS, AND PERSPECTIVES

CHAIR:

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Transcranial current stimulation (tCS) is a non-invasive brain stimulation technique based on the application of weak direct or alternating currents (tDCS, tACS) via scalp electrodes. Importantly, tCS can modulate the level and timing of spontaneous neuronal activity during the stimulation itself (online effects) but also produce lasting changes in cortical excitability beyond the period of stimulation (offline effects). To employ tCS for the investigation of neuronal oscillations and their function in cognition, it needs to be combined with recording methods like MEG or EEG. Tuned to detect very small current/voltage changes, however, these techniques are strongly challenged by stimulation artifacts being orders of magnitude larger than the brain signals of interest. While sequential stimulation and recording circumvents these problems, very recent methodological advances now made concurrent tCS-MEG and tCS-EEG feasible as well. This sets the stage for an entire new set of experimental approaches that can causally interact with spontaneous neuronal oscillations (e.g., by entrainment) while studying their immediate impact on neuronal processing, perception and behavior. The speakers of this symposium will not only present pioneering research using concurrent tCS-MEG and tCS-EEG but will also discuss the associated technical challenges and their solutions.

SIMULTANEOUS IN VIVO ASSESSMENT OF LARGE-SCALE CORTICAL FIELD ACTIVITY DURING TRANSCRANIAL ELECTRIC STIMULATION: PERSPECTIVES AND LIMITATIONS

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The ability to perturb or modulate brain physiology using non-invasive brain stimulation techniques, such as transcranial electric stimulation (TES), motivated a wide range of experimental work aiming at identifying causal links between brain structures, physiology and behavior. However, the direct effects of extracephalic electric currents on brain oscillatory activity remained unknown due to interference with stimulation-dependent electromagnetic artifacts that impede reliable neurophysiological recordings. Recently, we overcame this limitation using whole-head magnetoencephalography (MEG) and synthetic aperture magnetometry (SAM) beamforming, an advanced mathematical approach for reliable estimation of large-scale neural population activity and spatially-selective noise reduction. Here we give an overview of the technical and physical limitations of this new strategy, and introduce our most recent findings suggesting for instance that electric currents delivered to the primary motor cortex (M1) have an

immediate effect on slow cortical fields (SCF, 0-4 Hz) as measured by slow cortical source activity generated in a widespread network of motor-task related brain areas correlating with motor task performance. Our studies exemplify that combination of whole-head magnetoencephalography (MEG) and non-invasive electric brain stimulation is a powerful tool to test some fundamental hypotheses related to the causal link between neuromagnetic activity of specific brain structures and human behavior.

COMBINING TDCS AND MEG: THE CARDIFF EXPERIENCE

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Transcranial electrical stimulation (tES) is a safe and relatively inexpensive method for modulating brain activity. While there have been demonstrations of its efficacy in both simple sensorimotor and complex cognitive tasks, the exact underlying neurobiological mechanisms of the technique are still a matter of controversy. Directly monitoring the effects of tES on brain activity using non-invasive neuroimaging should allow a more complete picture of the techniques's effects. While both EEG and fMRI/MRS have been used in parallel with tES, its inclusion into the typical Magnetoencephalography (MEG) lab presents a number of unique challenges. Here we present pilot work showing the effects of tES in both pilot noise recordings and a dual-task paradigm, demonstrating the effects of both electrode montage and hypothesised active brain regions on MEG's ability to directly measure tES-induced changes in brain dynamics.

PROBING OSCILLATORY ACTIVITY IN THE VISUAL SYSTEM WITH TDCS/MEG AND TACS/MEG

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Neuronal oscillations at different frequencies subserve distinct functions in neuronal communication: In the visual cortex, alpha oscillations (8-12Hz) reflect a top-down driven 'pulsed inhibition' of task-irrelevant stimuli, whereas gamma oscillations (40-100Hz) rather reflect bottom-up driven stimulus processing. In this framework, alpha oscillations rhythmically modulate visual cortex excitability to suppress gamma oscillations, thereby actively controlling visual information processing. Transcranial current stimulation (tCS) of the visual cortex together with concurrent MEG recordings allows us for the first time to causally probe the relationship between cortical excitability and oscillatory dynamics directly at the site of stimulation. Our approach is two-fold: Firstly, online tDCS (anodal or cathodal) is used to transiently increase or decrease visual cortical excitability while subjects process visual stimuli known to produce robust gamma power increases. We hypothesized that tonic tDCS-induced increases/decreases in cortical excitability boost/reduce the bottom-up drive from the visual stimulus. Secondly, low-frequency tACS is used to entrain alpha oscillations and thus transcranially manipulate the degree of pulsed inhibition. We hypothesized that alpha-tACS produces a rhythmic modulation of stimulus-induced gamma power phase-locked to the entraining alpha frequency. We will discuss results from these two ongoing studies as well as technical challenges and solutions for handling tCS-artifacts in MEG recordings.

COMBINING EEG AND TRANSCRANIAL ALTERNATING CURRENT STIMULATION

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Transcranial alternating current stimulation (tACS) is a relatively recent method to stimulate the brain with weak sinusoidal currents. It has been demonstrated that tACS can modulate perception as well as other cognitive processes. To assess the immediate effects of tACS on brain activity, recording of EEG or MEG would be desirable at the time of stimulation. Unfortunately, however, the electric current flow caused by tACS introduces a relatively strong artefact in electrophysiological measurements. One way to circumvent the artefact is to record EEG before and after tACS in order to assess the after-effects. Using this approach, we were able to demonstrate that tACS at individuals' EEG alpha frequency is able to modulate the amplitude of EEG alpha oscillations for a duration of at least 30 minutes after the end of tACS. In addition, we will introduce procedures for removal of the artefact and will discuss problems that are associated with these approaches.

S11: STATES OF CONSCIOUSNESS IN HEALTH AND DISEASE: NEW APPLICATIONS FOR MEG IN RESEARCH, IN THE CLINIC AND AT HOME

CHAIR:

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MEG has struggled for many years to find a significant role in neuroscience research and clinical practice. The adoption of MEG by big laboratories has led to important basic research studies using either MEG alone or the combination of MEG with other techniques like EEG, TMS and fMRI. However, a strong impact of MEG in clinical practice remains largely confined to epilepsy and the identification of eloquent cortex. The symposium will bring together MEG studies of different states of consciousness ranging from anaesthesia, sleep and conditions where epilepsy, stroke and injury disturb these states. The presentations will highlight the opportunities provided by the exceptional combination of relatively good spatial and excellent temporal resolution of MEG. The first presentation will provide the basic framework that energy expenditure establishes for brain operations. Each of the other four presentations will provide examples of either basic research with MEG in dissociative anaesthesia, pathological origins of slowing of electrical

activity, changes in sleep and finally in ways MEG can help track cortical dysfunction in chronic stroke and dementia and help define unobtrusive but effective and personalized home-monitoring of epileptic patients, returning to the question of energy consumption and the contrasting electrophysiology and hemodynamic findings.

BRAIN ACTIVITY IN DISSOCIATIVE ANAESTHESIA: MEG RESULTS FROM IN HEALTHY PARTICIPANTS

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The action of anaesthetics on the brain provides an unprecedented opportunity to investigate the neural correlates of consciousness. Critical events occur in the transition between consciousness and unconsciousness for a wide range of anaesthetic agents suggesting that anaesthetics may all act through a final common pathway. While promising such work is restricted in scope by largely focusing on the actions of inductive agents using electroencephalography (EEG). Because the majority of inductive agents act principally through the agonism of inhibition and the assessment of functional connectivity using EEG is almost always calculated in sensor space the generalizability of the findings and the specificity regarding alterations in cortical activity are necessarily limited. Using higher resolution functional techniques such as MEG is necessary. We will present novel results in which MEG activity was recorded in healthy participants anaesthetized to loss of response using the anaesthetic noble gas Xenon. Xenon, a dissociative anaesthetic agent, is thought to work principally through the antagonism of cortical excitation and thus represents a different mode of action compared to agents typically studied. These results will highlight the unique role that he MEG will play in characterising drug-induced alterations in conscious brain activity.

ELECTROPHYSIOLOGICAL SLOWING AS A BIOMARKER OF LOCALIZED CORTICAL DYSFUNCTION

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Electrophysiological slowing is a common finding in cases of structural damage to the central nervous system, but its clinical applications have been limited, largely by the relative lack of specificity of the finding, as it can be present regardless of the underlying cause of the damage (i.e. stroke, tumour, TBI). However, advances in time-series analysis and source localization of MEG signals have re-established slowing as an important biomarker of localized abnormality in tissue that is structurally intact but functionally compromised, due to hypoperfusion, disconnection, synaptic damage, or other factors. We present methods for the localization and quantification of focal slowing in MEG, using beamformer-based reconstruction of virtual channel time series on the voxel level. In a sample of chronic stroke patients with aphasia due to left-hemisphere infarcts, we demonstrate that spontaneous electrophysiological activity is significantly slowed in perilesional cortex, compared to both healthy control subjects and to other regions of the same patients' brains. We compare spectrum-based (e.g. relative power in delta and theta bands) and nonlinear analysis methods (e.g. multi-scale entropy), showing that although there is a strong correlation between both, nonlinear measures may be more sensitive to lesion-induced abnormalities and less sensitive to effects related to healthy aging.

EEG AND MEG DYNAMICS OF SOUND AND SAFE SLEEP

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Although sleep consolidation demands reduced responsiveness to external stimuli, sleepers maintain a level of stimulus processing that allows responding to potentially dangerous environmental signals. The mechanisms underlying these contradictory functions are unknown. MEG tomographic recordings showed substantial and spatiotemporally differentiated activity in NREM sleep periods devoid of large graphoelements. They highlighted a small area in left dorsomedial prefrontal cortex as a hub of strong gamma band activity; increasing further as NREM sleep deepens and greatly expanding during REM. EEG recordings demonstrated that K-complexes (a) always interrupt any ongoing spindle, (b) are often (70%) followed by spindles of invariably higher frequency than the sporadic ones and (c) contain a brief oscillation in the high theta band, which consistently moves in space (backward) and time (increase in frequency). Correlations indicated that spindles are not directly evoked or depressed by K-complexes, but rather emerge in parallel to them and have a refractory period of ~4 seconds. Both MEG and EEG data support the hypothesis that in NREM-2 sleep operate cognitive processes which assure that we are safe and so can continue to sleep.

MEG FOR PERSONALIZED MEDICINE: IN THE HOSPITAL AND AT HOME

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MEG provides access to a unique spatiotemporal window that can resolve events in the brain at near millimetre spatial accuracy and at sub-millisecond temporal resolution. At the same time it can map activity across the entire brain over minutes or hours. This capability has been used with good effect in basic research but surprisingly in only few clinical applications. We will demonstrate two promising and contrasting applications of tomographic analysis of sleep MEG recordings. The first application, within a hospital environment, provides a quantifiable measure of sleep spindle activity for predicting outcome and/or monitoring rehabilitation after stroke. The second example use tomographic analysis of MEG data to optimize and personalize continuous monitoring of patients at home with simpler and more widely available devices. Finally, tomographic estimates of brain activity will be used to quantify the energy consumption in different sleep stages and contrast these MEG-based findings at different frequency bands to estimates of energy consumption from hemodynamic methods. Examples will be drawn mainly from recent results from the project ARMOR, partially funded by the European Commission under the 7th Framework Program with grant number 287720.

S12: WHAT IS DECODING AND WHAT CAN IT BRING TO NEUROSCIENCE?

CHAIR:

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Over the last decade, supervised learning – commonly referred to as decoding in the field of neuroscience – has emerged as a new tool to detect statistical effects in experimental data. The use of decoding techniques has first appeared in functional MRI, coined as Multi-Variate (or Multi-Voxel) Pattern Analysis (MVPA). Over the last few years, MEG and EEG research has caught up on this trend leveraging the ability of revealing the fast temporal dynamics of neural processes. This symposium aims to give a general introduction to decoding methods, warn about the potential caveats, advertise good practices and present some recent work in the field of neuroscience where decoding has proven to be successful.

DEFINITION, VALIDATION AND EXAMPLES OF DECODING WITH M/EEG

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The term "decoding" refers to the problem of predicting from neuroscientific data a target variable. It can be the behavior of the subject such as the reaction time or the type of response. It can be a descriptor of the stimulus (color or orientation for visual stimuli), the type of task or condition performed by the subject. From a statistical learning perspective it amounts to a supervised learning problem and from a practical point of view it allows to test for the presence of an effect of interest in the data leveraging the ability of the "decoder" to combine information from multiple features. The decoder is said to be multi-variate and in the context of MEG/EEG it can basically amount to predicting from all sensors jointly. I will first review the different categories of decoders (classification vs. regression vs. ordinal regression) and shed some lights on popular ones such as SVMs. I will then discuss the issue of validation before presenting some recent results obtained on 2 MEG studies related to consciousness and visual perception. In both studies specific features of decoders are used: namely the ability of the decoder to generalize its prediction over time and reveal detection thresholds.

INTERPRETATION OF WEIGHT VECTORS OF DECODING MODELS

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Multivariate neuroimaging data is often analyzed with respect to external variables (targets) such as experimental condition, stimulus properties or behaviour. Models expressing the data as a function of the targets are called encoding models, while models reversing this relationship are called decoding models. Parameters of decoding models indicate the measurement channels informative with respect to the targets. However, being a function of both the signal and noise content at each channel, they do not allow determining the origin of the neural processes associated with the targets, and may assign significant weight to channels unrelated to the targets, while giving insignificant weight to a proportion of channels actually related to the targets. In contrast, encoding models assign significant weights only to channels related to the targets, and are therefore interpretable with respect to the brain processes of interest. We demonstrate the differences between weight vectors of encoding and decoding models using illustrative examples, simulations, and analyses of two real neuroimaging datasets. Moreover, we propose a procedure for transforming linear decoding models into corresponding linear encoding models.

SEARCHING FOR BIOMARKERS IN ATTENTION DEFICIT AND HYPERACTIVITY DISORDER

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One of the uses of decoding to inform neuroscience lies in the search for diagnostic and prognostic biomarkers. Here we present work showing how neuroimaging data can help provide objective biomarkers for Attention Deficit and Hyperactivity Disorder (ADHD)- a disorder which currently relies solely on clinical diagnosis. ADHD persistence into adulthood is about 30%, affecting 2-3% of all adults and thus presenting a major public challenge. We acquired MEG and fMRI data on 63 typically developing volunteers and 55 adults with DSM-5 diagnosed ADHD during a task-free paradigm. We then used a combination of machine learning methods and connectivity measures in order to find and interpret the patterns that best discriminated between the two groups. We further explored the role of psychostimulant medication and common comorbid disorders in moderating the neural features associated with ADHD.

TIME-RESOLVED DECODING

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In fMRI, decoding is typically applied to classify static activation patterns. However, MEG and EEG excel in providing a time-sensitive picture of brain activity. Thus, to fully exploit MEG/EEG data, decoding approaches should be time-resolved. We have applied MEG decoding to investigate the earliest latencies at which there is sufficient information to discern single-trial responses to different low-level visual features and found that such information is available in the early visual cortices already 50 ms after the stimulus on-set. On the other hand, the high temporal resolution of MEG can also be utilized by decoding oscillatory brain activity. We have developed a method to classify on-going brain activity and applied it to MEG recordings comprising short blocks of auditory, visual and tactile stimulation as well as rest. The algorithm predicted the stimulus/rest class with an average accuracy approaching 70% (chance level 25%) using data from 4-s windows and yielded features that can be readily interpreted in neurophysiological terms.

DECODING SEMANTICS FROM PHRASES AND SENTENCES USING MAGNETOENCEPHALOGRAPHY

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Semantic composition is the act of creating higher order meaning by combining the meanings of single words, a crucial part of communication and comprehension. Though we have some understanding of how people process and represent the semantics of single words, we do not yet fully understand the neural processes that govern semantic composition. Because semantic composition is rapid (<0.5s per word) MEG is a great tool for capturing these compositional processes at work. In this talk I will describe our recent progress towards decoding the semantic content of sentences from MEG data. Inspired by previous work, we represent each word's meaning with a vector of statistics culled from a large text corpus. We explore how sentence structure and the semantic predictability of the sentence impacts our ability to decode these vectors from MEG data.

S13: NOVEL DEVELOPMENTS IN TRANSCRANIAL MAGNETIC STIMULATION COMBINED WITH ELECTROENCEPHALOGRAPHY

CHAIRS:

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Transcranial magnetic stimulation (TMS) combined with electroencephalography (EEG) represents a powerful technique for directly and non-invasively assessing cortical excitability and connectivity in humans. The combination of TMS-EEG has been widely used in basic neuroscience and has recently gained importance in investigating several clinical conditions. The aim of the proposed symposium is to gather experts from world-class research groups and to present the latest developments of this tool. Six speakers will present cutting-edge novel findings covering a broad variety of topics ranging from tool development to basic and translational aspects of TMS-EEG applications. Specifically, in this symposium we will present methods for analyzing TMS-evoked EEG data, classical applications on cortical inhibition, TMS-tuned brain oscillations, brain connectivity and clinical applications for neurological as well as psychiatric disorders. In conclusion, we think that this symposium proposal would make a timely and important contribution to the Biomag 2014 conference since, almost twenty years after its first implementation, TMS combined with EEG is now ready to be tested as a standard tool of research as well as clinical practice. The chairs have extensive experience on TMS-EEG and in coordinating events: http://becs.aalto.fi/en/events/tms_factory/ .

METHODS FOR STUDYING TMS-EVOKED EEG DATA

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Transcranial magnetic stimulation (TMS) is a non-invasive technique that when combined with electroencephalography (EEG) allows one to study cortical excitably and connectivity. However, TMS can evoke large artifacts in EEG, which may greatly alter data interpretation. In this talk, I will present two methods based on independent component analysis (ICA) for studying the TMS-evoked EEG responses. These methods are capable of removing and suppressing large artifacts, making it feasible, for instance, to study language areas with TMS-EEG. After solving the artifacts problem, I will present how beamformer can be used for localizing cortical sources and how the methods based on ICA may improve the source localization. The methods are tested on simulated data and real data collected from different brain areas, such as, the motor cortex, the dorsal premotor cortex, and Broca's area. These methods provide new solutions for both basic and clinical research on TMS-evoked EEG data from different brain areas.

ASSESSING THE ELECTROPHYSIOLOGICAL CORRELATES OF CORTICAL INHIBITORY MECHANISMS THROUGH COMBINATION OF ELECTROENCEPHALOGRAPHY WITH TRANSCRANIAL MAGNETIC STIMULATION

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Assessing the integrity of the human brain circuitries is an overarching aim of the modern human in particular in relation to understanding the pathophysiology of debilitating disorders. An emerging and powerful method for assessing the human brain circuitry is the combination of transcranial magnetic stimulation with electroencephalography (TMS-EEG) which allows for in vivo and non-invasive assessment of specific brain circuitries in health and disease. In this talk, TMS paradigms of long interval cortical inhibition (LICI) and cortical silent period (CSP) will be introduced. LICI and CSP paradigms, when applied to the motor cortex, are suggested to reflect the integrity of gamma-aminobutyric acid (GABA)ergic mechanisms in the motor system. In these paradigms, cortical inhibition is classically evaluated through assessing the suppression of electromyography (EMG) recording at the periphery. By combining TMS-EEG and EMG, we have conducted a series of studies to go beyond the peripheral (i.e., EMG) correlates of inhibitory mechanisms and introduced potential EEG indices of inhibitory mechanisms in both motor and non-motor regions of the cortex. Furthermore, we have begun to apply TMS-EEG technique to evaluate the integrity of inhibitory mechanisms as a function of change in brain state. This talk will review our journey/findings to date.

EEG/MEG-RHYTHMS OF ATTENTIONAL SELECTION TARGETED BY FREQUENCY-TUNED TMS TO MODIFY PERCEPTION

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Brain oscillations reflect interactions between neuronal elements which functionally assemble through synchronization in specific frequency bands, depending on the state of the brain and on the task that is currently being executed. This gives rise to brain rhythms that can be measured on the scalp by electroencephalography (EEG). Transcranial magnetic stimulation (TMS) can be used to stimulate cortical areas in rhythmic pulse-trains, at frequencies that characterize EEG-signals. This raises two intriguing questions: Could frequency-tuned TMS be used to transiently entrain brain oscillations, and would this result in behavioural consequences? My talk covers (1) EEG-signatures that carry information on the excitability of visual cortex (amenable to attention control) and predict perception of an upcoming visual event. It then addresses the questions whether (2) these signatures can be transiently entrained by frequency-tuned rhythmic TMS, and whether (3) this alters perception in expected directions, i.e. in line with the proposed functional roles of these oscillations in perception and attention. The data will help to illustrate the contribution of TMS-EEG to the study of the causal role of brain oscillations in perception and cognition, with implications for understanding TMS actions.

EXPLORING HUMAN BRAIN CONNECTIVITY, EXCITABILITY AND PLASTICITY WITH TMS-EEG

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Most neuroscience techniques traditionally used in humans, such as EEG, MEG, fMRI and fcMRI, passively measure brain activity. However, when combined with noninvasive brain stimulation techniques such as Transcranial Magnetic Stimulation, these brain imaging techniques can be used to causally explore the functional network architecture of the human brain, and its alterations in disease states. Furthermore, the combination of these techniques can also be used to assess the effects of different brain stimulation protocols, thereby permitting the development of more refined treatment protocols. Here, we show that continuous theta-burst stimulation to primary motor cortex produces widespread and band-specific changes in EEG functional connectivity measures, with alterations in graph theory metrics. We also show how TMS-EEG measures provide evidence of increased cortical excitability in patients with disorders of neuronal migration and active epilepsy, and that this hyperexcitability is more prominent in regions with abnormal resting-state fMRI functional connectivity. Finally, we show how TMS-EEG metrics of plasticity can be used to assess the differential effects of stimulation in healthy older adults and patients with Alzheimer's disease. Such measures provide unique insights into brain function in healthy subjects, and may lead to development of novel biomarkers in a variety of diseases.

QUANTIFYING CORTICAL EEG RESPONSES TO TMS IN (UN) CONSCIOUSNESS

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We normally assess another individual's level of consciousness based on her/his ability to interact with the surrounding environment and communicate. However, we know that consciousness can be entirely generated within the brain, in the absence of any interaction with the external world, as while we dream. Yet, to this day, we lack an objective measure of the level of consciousness that is independent of processing sensory inputs and producing appropriate motor outputs. Theoretically, consciousness is thought to require the joint presence of functional integration and functional differentiation, otherwise defined as brain complexity. A novel method based on the compression of the electroencephalographic (EEG) spatiotemporal pattern in response to Transcranial Magnetic Stimulation (TMS) has been recently employed to empirically test this theoretical prediction in wakefulness as well as during physiological (sleep), pharmacological (anesthesia) and pathological (brain injury) loss of consciousness. This approach invariably shows that the complexity of the cortical response to TMS collapses when consciousness is lost during deep sleep, anesthesia and vegetative state, while it recovers when consciousness resurges in wakefulness, during dreaming, in the minimally conscious state or locked-in syndrome. This represents a first step towards a robust assessment of unresponsive individuals whose level of consciousness is unknown.

S14: THE FUNCTIONAL ROLE OF CROSS FREQUENCY COUPLING

CHAIRS:

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Based on animal research and human studies it has been proposed that cross-frequency coupling (CFC) plays a fundamental role in organizing the temporal dynamics of neuronal computation. High frequency oscillations (30-100 Hz gamma band) have been associated with local neuronal processing, whereas low frequency oscillations (5-14 Hz, theta and alpha band) are typically associated with top-down control. Numerous studies point to a coupling between the phase of the slower oscillations and the power of the faster oscillations. The aim of this symposium is to discuss the mechanistic and functional role of cross-frequency coupling and to report evidence of its non-invasive observations using MEG. This will be done by comparing animal and human data in order to generalize over species. Further recent methodological advances will be discussed in the context of concrete paradigms and resting-state, spontaneous brain activity.

DYNAMICS OF CROSS-FREQUENCY COUPLING IN THE RESTING & ACTIVE STATES

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During the past decade, resting-state networks have been identified with fMRI and more recently, using MEG imaging. Yet, the neurophysiological mechanism explaining the production of these organized fluctuations remains to be uncovered. Here we show non-invasively with MEG source imaging that the nested dynamics of neural oscillations provide a support for long-range, default connectivity in the resting brain. In particular, we confirm that the occurrence of local high-frequency neural oscillations is coupled with the phase of slower fluctuations and demonstrate that it is a ubiquitous phenomenon across the human brain. We further show that this nesting mechanism of phase-amplitude coupling between neural oscillations accounts for the correlated variations of imaging signals from different brain regions that have been observed using other techniques in the resting brain so far. Overall, our results suggest that the mechanisms that reveal the brain's resting-state networks with fMRI are based on the cross-frequency coupling between the phase of low-frequency components and the amplitude of high-gamma oscillatory fluctuations. We will discuss further this generic principle with experimental data illustrating how ongoing resting-state brain dynamics are perturbed by sensory stimulation.

COUPLING BETWEEN THETA PHASE AND GAMMA POWER IN THE HIPPOCAMPAL NETWORK

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Cross-frequency coupling between theta phase and gamma power is seen in the hippocampus and its main cortical input, the entorhinal cortex. Such coupling may be important for integrating cell assemblies across the regions during memory processing. Past work revealed interactions between theta phase and gamma power in two distinct frequency bands, slow (~40 Hz) and fast (~80 Hz) gamma. In this lecture, I will present new data suggesting that coupling between theta and slow gamma facilitates selection of cell assemblies coding information that is being recalled from memory storage. I will also present new findings that suggest that coupling between theta and fast gamma promotes compression of sequences of spatial memory representations, which may be important for memory encoding.

MEASURING DIRECTIONALITY BETWEEN NEURONAL OSCILLATIONS OF DIFFERENT FREQUENCIES

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It is well established that neuronal oscillations at different frequencies interact with each other. In particular, the phase of slower oscillations modulates the power of faster oscillations: phase-amplitude coupling (PAC). Examples are alpha phase to gamma power coupling (Osipova et al, 2008) and theta phase to gamma power coupling (Belluscio et al, 2012). We here ask if the phase of slower oscillations drive the power of faster oscillations or if the power of the faster oscillations drive the phase of slower oscillations? In an attempt to answer this question, we developed a new measure to estimate the cross-frequency directionality (CFD). This measure is based on the phase slope index (PSI) between the slower oscillations and the amplitude envelope of the faster oscillations (Nolte et al, 2010). To our surprise, we found that the amplitude envelope of gamma oscillations is leading slower oscillations in theta and alpha bands. Our finding poses a challenge to theories suggesting that theta and alpha oscillations modulate processing reflected in the gamma band. Rather, it seems as if gamma band activity modulates the phase of the slower oscillations.

ALPHA AND GAMMA-BAND OSCILLATIONS DURING WORKING MEMORY: NETWORKS, FUNCTION AND DEVELOPMENT

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The ability to gate relevant information is strongly related with an individual's ability to maintain information in working memory (WM). Recent theoretical work suggests that cross-frequency coupling (CFC) between the phase of alpha oscillations and the amplitude of gamma-band activity may reflect bursts of high-frequency activity which occur at preferential phases of the alpha rhythm. According to this hypothesis the CFC between alpha oscillations and gamma-band activity may support the selective read-out of relevant information, however, direct evidence for this relationship remains unclear. To examine this hypothesis we recorded MEG data during a WM-task in which participants were required to maintain task-relevant WM-items and to inhibit distractors. Our results suggest that the gating of task-relevant information and inhibition of distractors during WM involves activity at alpha(10-14Hz) and gamma (30-100Hz) frequency ranges. More specifically, our data show that alpha oscillations contribute to the inhibition of distractors by modulating the amplitude of distractor-related gamma-band activity during WM-maintenance. Finally, our data suggests that developmental changes in alpha and gamma band activity as well as their CFC also account for age-related changes in distractor-inhibition and WM-capacity.

S15: FUTURE PERSPECTIVES ON MAGNETOCARDIOGRAPHY

CHAIR:

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Research on magnetocardiographic diagnosis has been being conducted with a long history. In many reports, magnetocardiography (MCG) has been proven to be quite useful in early-stage diagnoses of various heart diseases like ischemic heart diseases, atrial fibrillation, flutters, conductive anomaly, sudden cardiac death, WPW syndrome, Brugada syndromes, fetal developmental disease, etc. Currently, several groups have been refocusing their MCG researches on large-scale clinical studies again.

In spite of its usefulness, it is not easy to find an MCG system in the clinical field. One of the reasons is that the interpretation of the analyzed results is not intuitive enough to medical doctors compared to the results of other

competing diagnostic imaging modalities such as echocardiogram, multi-detector CT, MRI, PET, SPECT. Thus, it is the time for providing more practical and easy diagnostic results and finding killer applications synergistically for the purpose of the survival of the biomagnetic medical technology in the clinical market.

In this symposium, we will discuss the issues on the principal advantages of MCG over other modalities, analysis for MCG sensitivity, development of an affordable MCG system, unrivaled fetal application and a frontier application of heart magnetic resonance.

DIAGNOSTIC OPPORTUNITIES OF THE MCG: CARDIAC CURRENTS, EXTRACORPORAL MAGNETIC FIELD AND NEW SENSOR CONCEPTS

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The magnetic field of the heart is associated to intra- and extracellular current flow during cardiac excitation. Numerical simulations and simultaneous measurements of MCG and ECG have shown that the signal patterns of surface ECG and MCG have no conclusive relation to each other. The reason is the distributed nature of cardiac current sources in tissue with anisotropic and inhomogeneous conductivity. Thus, additional structural information on cardiac sources and tissue can be obtained from the MCG. MCG is limited by the spatial separation between cardiac sources and SQUIDs. The number of independent parameters that can be reconstructed from the MCG is considerably lower than the number of channels in a multichannel Low-Tc SQUID system. However, useful diagnostic information can be found in general structural properties of MCG maps and time series. By changing the target from current reconstruction to identification of pathologic cardiac conditions, MCG might be a valuable tool in cardiac diagnostics. Recent developments both in high-Tc SQUIDs and in room-temperature operated optical magnetometers open the possibility for measuring closer to the sources with less experimental effort, so that main barriers for the clinical application of the MCG can be lowered.

ASSESSING SENSITIVITY AND RESOLUTION OF MCG AND ECG

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MCG and ECG detect cardiac electrical activity in a complementary way. In this work, we characterize the sensitivity and resolution of MCG with the help of numerical simulations and resolution analysis. We also assess the benefit of combining MCG and ECG.

A realistically-shaped volume conductor model was built using the boundary element method, and lead-field matrices for both modalities were assembled. Sensitivity was assessed in terms of L2 norm of the sensor topographies, and source-reconstruction capability was assessed via the point-spread function (PSF) of the linear minimum-norm estimator. Both assessments were done globally, for all source regions.

Overall, MCG showed higher sensitivity to tangentially-oriented than to normally-oriented sources, whereas BSPM was relatively more sensitive to normally-oriented sources. Comparing the modalities, MCG was relatively more sensitive to anterior tangential activity, while BSPM was more sensitive to anterior normal activity and overall posterior activity. The PSF analysis results reflected the sensitivity distributions: with MCG the anterior tangential activity was better localized and the corresponding source estimate was less spread compared to BSPM, whereas BSPM performed relatively better with posterior and normal sources. When MCG and BSPM were combined, localization errors and spreads were smaller and more evenly distributed.

VOLTAGE-BIASED SQUID MAGNETOMETER BASED 36 CHANNEL MAGNETOCARDIOGRAPH SYSTEM

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Recently, a voltage-biased direct readout dc SQUID magnetometer with a large junction shunt resistance was reported to have a very nice noise performance. In this study, a 36 system based on the magnetometer was set up in a magnetic shielded room for biomagnetic measurements. The shunt resistance RJ is 33 Ω or 12 Ω with flux-to-field coefficient $\partial B/\partial \Phi$ of 0.57 nT/Φ_0 or 1.5 nT/Φ_0. 51 SQUID magnetometers were measured and calibrated with Nb shielding tube in a liquid helium tank, and the average field white noise of 7 fT/√Hz. To suppress the external interference, first-order and second-order gradiometer were constructed with three layer SQUID devices, including 36 signal channels, 12 reference channels and 3-axis magnetometer for compensation. A multi-channel direct readout electronics was also developed to adjust the SQUID working parameters and FLL control states. The system was set up in a magnetically shielded room and the 36 channel adult MCG signals and imaging were first obtained in SIMIT.

REALIZING THE PROMISE OF FETAL MAGNETOCARDIOGRAPHY

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Over the last decade, we and other groups have shown that fMCG can significantly aid in the diagnosis and clinical management of the major forms of serious fetal arrhythmia, such as supraventricular tachycardia and AV block. FMCG is also able to detect repolarization abnormalities, such as QT prolongation and T-wave alternans in fetal long QT syndrome, which cannot be diagnosed at all by ultrasound. In this presentation, I will review the efficacy of fMCG for evaluation of fetal heart rate and rhythm, based on our study of more than 400 fetuses with fetal arrhythmia, congenital heart disease, and other high-risk conditions. Despite considerable scientific and clinical progress, the dissemination of fMCG has been limited by the high cost of SQUID magnetometer technology. We are optimistic, however, that the recent breakthrough in atomic magnetometry can overcome this problem. This new technology is far less expensive than SQUID technology, and may allow the promise of fMCG and other biomagnetism applications to be fully realized.

HEART MAGNETIC RESONANCE

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I suggest a novel idea, heart magnetic resonance (HMR), to be applied to development of a medical instrument localizing an abnormal myocardial excitation in hearts.

The main idea of HMR is to match the proton magnetic resonance frequency to the specific frequency of the abnormal heart activity so that we could find the position of the reentry current by using the magnetic field gradient spatial coding method in the conventional magnetic resonance imaging.

In this presentation, we demonstrate the idea of HMR by conducting a computer simulation based on a realistic heart model and experimental parameters in SQUID-based micro-Tesla NMR.

S16: FROM NEURONS TO BEHAVIOR: ADVANCES IN COMPUTATIONAL NEURAL MODELING TO INTERPRET MEG/EEG SIGNALS

CHAIR:

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The last decade has experienced a revolution in our ability to image the brain from the cellular and circuit level, with techniques like 2-photon imaging and optogenetics animal systems, to the whole brain in humans with advances in fMRI, DTI and MEG/EEG. However, bridging between these scales continues to be challenging. Recent advances in computational neural modeling are proving to be a powerful, non-invasive and inexpensive tool that can provide the necessary interpretive links between behaviorally relevant human signals and their underlying neural mechanisms. In this symposium, we present recent advances in computational modeling methods to interpret MEG/EEG data using a variety of modeling techniques and statistical methods. Our complimentary approaches bridge scales from single cells to whole brain simulations in the context of healthy function and disease processes.

INTERACTIONS BETWEEN CORE AND MATRIX THALAMOCORTICAL PROJECTIONS IN HUMAN SLEEP SPINDLE SYNCHRONIZATION

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Sleep spindles are prominent thalamocortical bursts of 10-15Hz oscillations lasting ~1s. They have been implicated in memory and disease, and their neurobiology at a circuit, synapse and channel level have been extensively studied in animals. Spindles measured with the electroencephalogram are largely synchronous and distributed, whereas those measured with the magnetoencephalogram are largely asynchronous and focal, leading to the hypothesis that the former are generated by the matrix thalamocortical system, and the later by the core. Here we tested this hypothesis with a computational neural model containing both matrix and core elements in the thalamus and cortex. The cortex included multiple patches realistically arranged on the folded cortical surface. We found that the core/matrix model reproduced the empirically observed topography, strength and coherence of EEG and MEG during spindles. Increasing the fan-out of thalamocortical connectivity in the matrix pathway while keeping the core pathway fixed led to increased synchrony of the spindle activity in the superficial cortical layers in the model. The core/matrix model explicitly represents the interaction of focal and diffuse thalamo-cortical systems, with readily obtained empirical predictions at multiple levels. This integration of focal with distributed information processing may be a general mechanism of thalamocortical physiology.

A MODEL FOR PHASE CODING IN THE VISUAL SYSTEM COORDINATED BY GAMMA ACTIVITY PHASE-LOCKED TO ALPHA OSCILLATIONS

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Recent MEG studies have demonstrated that gamma activity is phase-locked to on-going alpha oscillations. We propose a specific mechanism for how these nested oscillations coordinate neuronal firing in early visual cortex. The key element of the mechanism is that the alpha activity provides bouts of inhibition preventing neuronal firing in a rhythmic manner. As the inhibition reduces within an alpha cycle, the most excitable visual representation will discharge. As the inhibition further reduces, the next representation will discharge and so forth. By this principle a set of visual representations is converted into a sequence encoded by the phase of the alpha oscillations. The level of excitation is set by visual contrast and top-down mechanisms reflecting figure-ground segmentation and attention. Further the individual representations are segmented by a fast GABAergic feedback that then produces the gamma oscillations. The proposed mechanism is inspired by investigations on phase coding in the rat hippocampus. We have implemented the mechanism in a physiologically realistic network model using conductance based model neurons. Our simulations provide proof-of-principle for a simple physiological mechanism based on gamma oscillations phase-locked to alpha oscillations that coordinates and prioritizes processing in the visual system.

BIOPHYSICALLY PRINCIPLED MODELS OF MEG/EEG CURRENT SOURCE SIGNALS REVEALS NOVEL MECHANISMS OF NEURAL RHYTHMS AND THEIR IMPACT ON FUNCTION

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Computational models to study the origin of human MEG/EEG signals have been developed at a variety of scales from networks of spiking neurons to neural mass and population representations. We have developed a

biophysically principled model of a laminated cortical circuit designed specifically to reproduce the primary current sources contributing to these signals (e.g. current dipoles), with units of measure directly comparable to the recorded data (nano-Ampere-meters). The model links the recorded macroscopic level activity to the microscopic cellular and circuit level dynamics. In this symposium, we present results showing that, in keeping the output of the model in close agreement with the data, we have derived novel hypotheses on the mechanistic origin of low frequency neural rhythms (alpha 7-14Hz, beta 15-29Hz and gamma 30-150Hz) measured with MEG. These predictions are being validated with invasive electrophysiological and optogenetic recordings in mice. Further, we will present our studies on the impact of these rhythms on function and recent results investigating changes with healthy and abnormal brain development in infants and children.

DYNAMIC CAUSAL MODELING: A MATHEMATICAL MICROSCOPE FOR THE OBSERVATION OF NEURAL SYSTEM TRANSMITTERS

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Over the past number of years, biophysical models of the brain have allowed experimental neuroscientists to pose mechanistic hypotheses regarding the neural architecture generating their empirical data. One such framework, known as Dynamic Causal Modeling (DCM) has been applied in the domains of fMRI, M/EEG and animal LFP studies, to investigate brain connectivity. We believed that this general approach could be developed to probe even finer grained physiological detail, down to the level of specific neurotransmitter activity at the synapse. In this talk I will propose DCM as a methodology for the assay of levels of important neurotransmitters and as a framework for understanding large scale brain networks and the algorithmic principles that they employ to perform cognitive functions.

Effectively I will demonstrate that it is possible to cross many scales of neurobiological description using data acquired non-invasively, thereby linking overt behaviour to its molecular components, providing a window on to the machinery of the human mind. I will specifically demonstrate DCM for MEG as a modality for assessing the synaptic mechanisms that are affected by cholinergic, GABAergic and dopaminergic drugs, in the performing brain

THE VIRTUAL BRAIN: DELIVERY PRACTICAL RESULTS FOR NOVEL CLINICAL APPLICATIONS

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For over 20 years, bright minds and ambitious projects have attempted to emulate the human brain across various scales of organization. Despite impressive efforts to bring in the latest and greatest computing power of massively parallel hardware, success hasn't yielded practical applications yet. To get practicality sooner, we are developing "The Virtual Brain", which takes a network approach on the largest scale: By manipulating network parameters, in particular the brain's connectivity, The Virtual Brain will simulate its behavior as it is commonly observed in clinical scanners (e.g. EEG, MEG, fMRI). The Virtual Brain will deliver the first open simulation of the human brain based on individual large-scale connectivity. Within the next 5 years, running on comparably tame hardware and right in your browser. In this talk, we will present the current state and future directions of The Virtual Brain and demonstrate how it can transform clinical therapy for brain diseases.

S17: BRAIN OSCILLATIONS AND NETWORK CONNECTIVITY IN TYPICAL AND ATYPICAL NEUROCOGNITIVE DEVELOPMENT

CHAIR:

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Magnetoencephalography has played a vital part in recent breakthroughs in our understanding of brain oscillations and their role in cognition and functional networks. This symposium will focus on the emerging field of MEG research into how brain oscillations develop throughout childhood and adolescence. Recent work on the development of neural oscillations and network connectivity in both resting-state and task-dependent networks will be highlighted. Relations between oscillations, networks and cognitive development will be discussed. Moreover, recent research exploring link between brain oscillations, functional network connectivity and developmental difficulties in clinical child populations will be presented. This symposium will offer novel vistas into neuromagnetic insights into the maturation of cortical network dynamics and developmental cognitive neuroscience.

GAMMA PHASE SYNCHRONY IN AUTISM SPECTRUM DISORDERS – A BIOMARKER FOR THERAPIES

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Recent observations in Autism Spectrum Disorders have resolved reduction in auditory evoked gamma-band oscillatory activity, and in particular measures of inter trial coherence (ITC). In parallel, emerging evidence links gamma-band oscillations to cortical local circuitry requiring a delicate balance of excitatory and inhibitory neurotransmitters (primarily glutamate and GABA). Deficits in such E/I balance have been proposed as part of the neurobiological basis of autism. Additionally, recent work has associated gamma-band activity measured by MEG with levels of neurotransmitters (especially GABA) measured in appropriate cortical regions by edited magnetic resonance spectroscopy. Very recent studies indeed document reduction in GABA levels, measured by MRS, in ASD populations, further cementing the neurobiological association between atypical GABA, atypical gamma-band activity and ASD. Results presented will review gamma-band activity from a large cohort of children on the autism spectrum, showing profound ITC deficits, as well as associated reductions in temporal lobe GABA. A case study of responsiveness of MEG measures of gamma-band activity to therapy with a GABA-B agonist will be presented from a recent clinical trial, along with a rationalized case for the use of MEG measures of

gamma-band oscillatory activity as stratification biomarkers for such treatments as well as sensitive indicators of response.

FUNCTIONAL CONNECTIVITY AND ENTROPY IN DEVELOPMENT

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As we mature, the brain becomes more adept at performing tasks, demonstrated through increased task performance and consistency, however the underlying neural correlates of development are less well understood. In this study we investigate both complexity (via entropy) and connectivity within multiple, well characterised brain networks, and how these effects change with age.

47 healthy volunteers aged 9 – 25 years took part. Subjects underwent a 5 minute resting state and two cognitive tasks, data recorded with a 275 channel CTF MEG system. Beamforming was used to reconstruct timecourses of source strength from large scale distributed networks (visual, motor, left and right fronto parietal networks). Canonical correlation analysis [1] was used to assess connectivity between two network nodes. Multiscale Sample Entropy (MSE) [2] was used to assess complexity within networks.

Functional connectivity was found to modulate significantly ($p<0.05$) with age, with reduced connectivity in younger participants. Effects were most pronounced in the motor network and left fronto-parietal network. Generally entropy was found to increase significantly ($p<0.05$) with age in all but the visual network, in agreement with [3]. MSE assesses entropy on multiple temporal scales; it was found that at short temporal scales entropy increases with age but at coarser temporal scales entropy decreased with age, thus highlighting the importance of high temporal resolution assessment.

Together these findings show that network dynamics, particularly in the fronto-parietal and motor networks, develop throughout adolescence, whereas the visual network dynamics appear stable from early childhood.

DISRUPTED BRAIN CONNECTIVITY IN ATYPICAL DEVELOPMENT: INSIGHTS FROM RESTING-STATE MAGNETOENCEPHALOGRAPHY

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Recent research has seen a surge in the study of connectivity between spatially separate, yet functionally related brain regions. Oscillatory synchrony is integral for the organization of intrinsic networks and for information processing, and abnormal neural synchrony has been demonstrated in neurodevelopmental disorders. The majority of research on intrinsic connectivity networks, however, has been performed using fMRI, and little is known about the electrophysiological correlates of functional connectivity at faster frequencies. This talk will present recent findings regarding intrinsic functional brain networks in pediatric populations using resting-state MEG. Atypical network organization in two clinical populations will be highlighted: children born very-preterm and adolescents with autism spectrum disorder (ASD). Our approach used source-resolved coherence of neuromagnetic oscillations as a measure of communication in distributed neural networks. We identified altered network coherence in clinical populations when compared to typically-developing matched controls. For example, adolescents with ASD exhibited frontal over-connectivity at high frequencies coupled to posterior under-connectivity to widespread brain areas in slower frequencies. Further, atypical network coherence differences were related to the putative functions of oscillations in specific frequency ranges. Overall, our results suggest that altered neural synchrony contributes to deficits in neurodevelopmental disorders.

AGE RELATED CHANGES OF MEG ALPHA AND GAMMA-BAND ACTIVITY REFLECT THE LATE MATURATION OF DISTRACTOR-INHIBITION DURING WORKING MEMORY MAINTENANCE

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Previous evidence highlights the importance of alpha and gamma oscillations in large-scale functional networks for the selection and maintenance of relevant information. To investigate developmental changes of activity in both frequency bands in relationship to age related differences in behavioral performance, MEG activity was recorded in a sample of participants aged between 12 and 24 years while they performed a delayed match to sample WM-task. The findings of this research show that young adolescents have a reduced WM capacity as compared to adult participants. This reduction in WM capacity in young adolescents was also associated with markedly decreased behavioral performances in the presence of distractors and with developmental changes in alpha and gamma band activity. Importantly, developmental changes in rhythmic activity at alpha and gamma frequencies were found only in the distractor condition, further highlighting the importance of alpha and gamma oscillations during distractor inhibition and the selection of relevant information. The results from the present study confirm previous evidence showing that alpha and gamma oscillations differentially contribute to the maintenance of information WM and provide important evidence for a functional relationship between the development of WM capacity, distractor-inhibition and rhythmic activity in the alpha and gamma frequency bands.

USING MEG TO INVESTIGATE CORTICAL BIOMARKERS IN CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER

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Autism spectrum disorder (ASD) is a behaviorally diagnosed neurodevelopmental disorder characterized, among other things, by abnormal cortical functional connectivity. We were interested in the spectral signatures of abnormal functional connectivity in ASD, and in whether such neurophysiological metrics were correlated with behavioral measures. To that end, MEG data were recorded during resting state, tactile vibrations on fingertips, and face processing paradigms. Long-range coherence was examined between functionally distinct cortical regions. Local interactions were examined within a functionally defined cortical region. We found patterns of both increased and reduced functional connectivity across cortical regions in ASD in different paradigms. During resting state, the properties of the network varied consistently with frequency band. During two of the paradigms,

tactile vibrations and face processing, we observed reduced local functional connectivity in the ASD group. These neurophysiological metrics correlated with behaviorally assessed ASD severity, and for the sensory task, also with sensory processing scores. Lastly, classification using these metrics achieved around 90% accuracy in blindly identifying ASD participants. Our studies suggest that local interactions that are likely mediated via inhibitory connections are reduced in ASD. The correlations between these neurophysiological metrics and behavioral ASD measures suggest a relevance to the etiology of ASD.

S18: CROSS-FREQUENCY COUPLING – METHODOLOGICAL CHALLENGES

CHAIR:

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Neural oscillations synchronize in different regimes such as delta, theta, alpha, beta, and gamma frequency bands. Synchronization occurs within local neural ensembles and between distant ensembles. It is modulated by task demands but also occurs at rest. (Changes in) neural synchrony can be considered a major carrier of neural information. Recent empirical findings suggest that oscillations at different frequency bands are not independent of each other but interrelate according to various forms of cross-frequency coupling involving the phase, amplitude or frequency of the signals. Robust assessment of cross-frequency coupling comes with challenges. All the participating speakers studied neural synchronization against this common background. For this symposium, speakers are explicitly asked to highlight modern-days approaches and discuss their pros and cons against the background of M/EEG-related confounders like volume conduction and poor signal-to-noise ratios. A broad range of methods will be presented, including bispectral analysis, phase-amplitude coupling, and the use of computational models to infer time-resolved amplitude-amplitude interactions. Such methodological advances are crucial for reliable detection of cross-frequency interactions and interpretation of experimental findings. Our speakers are therefore also asked to discuss the potential implications of their cross-frequency measures for our general understanding of neural functioning.

CROSS-FREQUENCY COUPLING AS A MEASURE OF BRAIN INTERACTIONS

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Nonlinear coupling measures like 1:2 phase locking or phase-amplitude coupling can be measured in single sensors with in general non-trivial results. Hence, as a coupling measure across sensors or estimated sources it may reflect a coupling between different neuronal groups or the result of mixing of nonlinear but independent sources. In this talk I want to present methods to construct cross-frequency coupling measures, which are not sensitive to mixtures of independent sources based on cross-bispectra. It will be shown that phase-amplitude coupling cannot be a relationship at two distinct frequencies. A reasonable estimator of this phenomenon can be expressed in terms of cross-bispectra, which require coupling between three different frequencies. For the study of brain connectivity the mixing problem of MEG data is very severe especially in the presence of mixed noise because in this case it is impossible to demix all sources. Since brain noise is largely Gaussian distributed, it is conceivable that for strictly nonlinear coupling measures as given e.g. by cross-frequency coupling measures a sufficient decomposition of sources is possible such that all cross-frequency coupling measures represent a meaningful estimation of brain connectivity. Both of these approaches will be compared for real MEG and EEG data.

CROSS FREQUENCY CORRELATIONS - WHEN DO THEY INDICATE COUPLING?

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Interactions between neural activity components at different frequencies have been proposed as an elegant mechanism to allow the integration of neural information processing across various timescales. Traces of this putative mechanism, termed cross frequency coupling, have been reported for various recordings of neural activity across species and experimental paradigms. However, many studies on cross frequency coupling fall short of mastering the technical difficulties of separating genuine cross frequency coupling from more general cross frequency correlations that arise due to non-stationarities of almost any kind in the data (e.g. all stimulus-driven activity). This talk reviews the mathematical prerequisites for a sound analysis of cross frequency correlations of the desired types and the analysis and experimental paradigms that allow the use of the term 'coupling'.

BI-PHASE LOCKING – A TOOL FOR PROBING NON-LINEAR INFORMATION TRANSFER IN THE BRAIN

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The bi-phase locking value (bPLV) is a direct extension of the well-known phase locking value (PLV) and can serve as tool for probing long rage cortical interactions for cross-frequency coupling as well as local activity. Due to its sensitivity to only non-linear interactions, it is robust to spurious synchronization arising from linear crosstalk, which is an especially useful property when analyzing data recorded by EEG/MEG. However, by expanding the space of potential interactions to the cube of possible sources and adding another frequency dimension, i.e. producing time by frequency-by-frequency maps, careful statistical testing of the results is necessary in order to avoid spurious results. In this presentation we will discuss the statistical properties of the bPLV under the null-hypothesis of purely random phases and non-parametric tests in case of arbitrary null-distribution of the signals phases. We will give an example of the application of bPLV to electrocorticography data during a motor task.

A COMPUTATIONAL MODEL OF CROSS-FREQUENCY COUPLING IN RHYTHMIC MOTOR CONTROL

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Extensive evidence suggests that beta-band (15-30 Hz) oscillations play a key role in human motor control. During rhythmic motor performance, beta-band oscillations are nested within the slower movement cycles. MEG data acquired during bimanual coordination revealed that this amplitude-phase coupling get stronger with motor learning while it gets weaker at higher movement frequencies when motor coordination becomes less stable. In this presentation I will consider a form of winnerless competition known as heteroclinic cycles as a potential model for cross-frequency coupling. Cortical activity can be modeled by an ensemble of coupled phase oscillators that robustly show heteroclinic cycles between cluster states in a broad region of parameter space. These switches between cluster states generate nested oscillations in their ensemble activity and I will discuss the role of the model parameters on the timing of the switching behavior. By coupling two ensembles together the model shows n:m frequency coupling at the movement frequency with beta-band oscillations nested within these slower time scales. The model agrees with the cross-frequency coupling observed in MEG recordings during bimanual coordination and may provide a potential mechanism for nested cortical oscillations in general.

ESTIMATING DIRECTIONAL CROSS-FREQUENCY COUPLING FROM TIME-FREQUENCY SPECTRA USING DYNAMIC CAUSAL MODELING

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When subjects perform a behavioral task, one can typically observe spectral modulations across different frequencies and brain regions. In order to understand how the activity of these regions is functionally related, most studies so far have focused on coupling within the same-frequency band and without specifying directionality. However, it is likely that the brain fully exploits its capacity for directional and cross-frequency interactions for information processing. We demonstrate how these interactions can be estimated from M/EEG data using dynamic causal modeling. The generative model for this consists of linear response functions that describe how time-frequency modulations are induced by connections within and between sources containing within and between-frequency coupling parameters. The Bayesian inversion scheme allows for a systematic comparison between models that differ in the configuration of connections within the network of selected brain regions. Subsequently, the directional cross-frequency parameters values of the most likely model can be assessed. We illustrate this procedure by looking at the movement-related beta and gamma power modulations of simultaneously acquired LFP and MEG data of Parkinson's disease patients. A promising future extension of the model would be to incorporate a neural mass model to bring the model closer to neurophysiology.

S19: MECHANISMS OF INTEGRATION/SEGREGATION IN THE RESTING BRAIN

CHAIR:

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Interaction estimated from spontaneous fluctuations of the BOLD signal provides spatially and temporally structured networks, namely resting state networks (RSN), appearing as large scale, topographically segregated functional systems [1]. However, while segregation complies with the functional specialization of RSN, effective behavior depends on the dynamic integration of sensory, motor, and cognitive functions at multiple spatial and temporal scales [2]. Actually, recent findings based on the study of spontaneous brain oscillations enrich the fMRI scenario with additional temporal and spectral features providing new insights on these integration/segregation mechanisms. In fact, theoretical models of neuronal pools as oscillators are supported by EEG and MEG, suggesting coexistence of functional segregation and dynamic integration. Preliminary studies suggest that they occur at different oscillation frequencies [3-4] and time epochs [3][5], with specific networks being more central and others more segregated. In this view, the mechanisms underlining integration/segregation will be discussed in this symposium, from models to architectures of large scale interactions.

DWELLING IN THE RICH CLUB: CONNECTOMIC DETERMINANTS OF BRAIN DYNAMICS

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Endogenous, "resting state" cortical dynamics reflect the interplay between recurrent activity in local neuronal populations and the influence of many cortical regions interacting through the structural connectome. Recent research has established that this structural connectome consists of a complex mosaic of local network motifs hung together through a backbone of densely interconnected "rich club" superhubs. In isolation, small network motifs highly constrain patterns of synchrony and dynamic instability amongst pairs and triplets of neuronal populations. Using large-scale simulations, we here show that these local motif dynamics indeed survive immersion into the network structure of the primate connectome. Furthermore, the rich club structure of this connectome plays a crucial role in orchestrating how these local dynamics are deployed across the brain. In particular, motifs supporting stable, synchronous dynamics are concentrated around the rich club, such that a stable dynamic core surrounds the structural core of the brain. In contrast, motifs supporting unstable dynamics, with rapid metastable patterns of activity, are distributed throughout the topological periphery of the brain. We provide a speculative interpretation of these results in terms of mood, perception and notions of interiority.

RAPID RESTING-STATE-NETWORK DYNAMICS

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The brain is intrinsically organized into large-scale resting-state-networks (RSNs) whose hemodynamic signature changes about every 10 seconds. Such slow dynamics are hardly compatible with the rapid dynamics necessary for the execution of mental tasks. The EEG topography remains stable for much shorter periods (~100 ms, the so-called EEG microstates). We hypothesized that the temporal dynamics of RSNs is much faster than the fMRI suggests and that the EEG microstates are their electrophysiological signature. Using simultaneous EEG/fMRI, we identified EEG microstates as the electrophysiological correlate of four fMRI RSNs (auditory, visual, self-referential, attention-reorientation). This direct link is surprising given that the temporal scales at which the EEG and fMRI signal are meaningful are two orders of magnitude apart. Subsequent wavelet-based fractal analysis revealed that this link could be established because the EEG microstates are mono-fractal and show scale-free properties across 6 dyadic scales from 256 ms to 16 sec. Their sequence is neither random nor determined but chaotic: it follows clearly defined rules without being predictable, analogous to how all natural languages follow a generative grammar. This is the key feature that permits the brain to rapidly adjust to unexpected events and to successfully interact with the environment.

MEASURING THE TEMPORAL, SPATIAL AND SPECTRAL DYNAMICS OF FUNCTIONAL CONNECTIVITY

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The topic of functional connectivity in neuroimaging is expanding rapidly and many studies now focus on coupling between spatially separate brain regions. These studies show that a relatively small number of large scale networks exist within the brain, and that healthy function of these networks is disrupted in clinical populations. To date, the majority of studies probing connectivity employ techniques that compute time averaged correlation over several minutes, and between specific pre-defined brain locations. However, evidence suggests that functional connectivity is non-stationary. Further, electrophysiological measurements show that connectivity is dependent on the frequency band of neural oscillations. It is also conceivable that networks exhibit a degree of spatial inhomogeneity, i.e. the large scale networks that we observe may result from the time average of multiple transiently synchronised sub-networks. This means that the next generation of neuroimaging tools to compute functional connectivity must account for spatial inhomogeneity, spectral non-uniformity and temporal non-stationarity. In this talk I will present a method to achieve this via application of windowed canonical correlation analysis to source space projected MEG data. I will show that, in a resting state MEG experiment, it is possible to detect multiple distinct spatio-temporal-spectral modes of covariation within the sensorimotor network.

DYNAMICS OF CROSS-FREQUENCY COUPLING IN THE RESTING & ACTIVE STATES

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During the past decade, resting-state networks have been identified with fMRI and more recently, using MEG imaging. Yet, the neurophysiological mechanism explaining the production of these organized fluctuations remains to be uncovered. Here we show non-invasively with MEG source imaging that the nested dynamics of neural oscillations provide a support for long-range, default connectivity in the resting brain. In particular, we confirm that the occurrence of local high-frequency neural oscillations is coupled with the phase of slower fluctuations and demonstrate that it is a ubiquitous phenomenon across the human brain. We further show that this nesting mechanism of phase-amplitude coupling between neural oscillations accounts for the correlated variations of imaging signals from different brain regions that have been observed using other techniques in the resting brain so far.

Overall, our results suggest that the mechanisms that reveal the brain's resting-state networks with fMRI are based on the cross-frequency coupling between the phase of low-frequency components and the amplitude of high-gamma oscillatory fluctuations.

We will discuss further this generic principle with experimental data illustrating how ongoing resting-state brain dynamics are perturbed by sensory stimulation.

ARCHITECTURE OF MEG FUNCTIONAL INTERACTIONS AT REST

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Recent MEG/EEG studies described the electrophysiological correlates of the resting state networks (RSN), showing that RSN seem to be functionally segregated at specific time epochs and for specific oscillation frequencies. However, integration among RSN coexists with segregation at different frequency bands (i.e the beta band), time instants and time scales. Although the number of RSN is relatively small, this multidimensional structure of communication might be the ground over which the brain faces the external world. Thus, with the aim at studying the architecture of communication at rest, we report here our recent results on the structure of within/across network interactions at the beta band. Betweenness centrality over time showed that specific networks are on average more segregated, while others are more central. Specifically, nodes from the Default Mode Network, the Motor Network and the Dorsal Attention Network seemed to be consistent hubs. Additionally, we found these three RSN as good classifiers of time epochs corresponding to peaks of global efficiency, differently from other RSN. These results point into the direction of a dynamic core network model in which the communication in the whole brain is ensured by the cross-network interaction realized through a continuous interchange of central networks.

S20: EVOKED AND INDUCED OSCILLATION IN THE AUDITORY, VISUAL AND SENSORIMOTOR SYSTEMS – MECHANISMS AND APPLICATIONS

CHAIRS:

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The presentations in this symposium provide a tour through the wide range of neuromagnetic oscillations, which are evoked and induced by auditory and visual stimuli at gamma frequencies, multiple rhythms of speech, and rhythmic sound and movements of musical beats. The authors provide insights into the neural generation mechanisms of auditory and visual evoked steady-state gamma oscillations. They introduce applications to research in psychiatry by demonstrating the effects of changing GABA level for the generation of gamma oscillations. They show how noise interacts with hearing and explain why hearing in noise becomes difficult in aging. Classical fear conditioning will be demonstrated with visual flicker evoked gamma oscillations. Brain oscillations induced by the various rhythms of speech provide explanations for the mechanisms of speech encoding. Moreover, cross-spectral interactions between brain oscillations recorded during listening to ongoing speech support a system of nested oscillators for the encoding and processing of speech. Perception of the beat rhythm in music interacts with the sensorimotor system for rhythmic movement, which has been studied with beta oscillations in MEG and EEG. Two studies address how sensorimotor oscillations change during development.

GABA AND THE AUDITORY STEADY-STATE RESPONSE

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Combined MEG measurements and MR spectroscopy have identified interesting relationships between oscillatory activity and brain metabolites. GABA concentration in the visual cortex is related to the frequency of gamma-band activity. Studies have not been published on auditory responses and GABA.

Forty-five individuals participated in an MEG and proton magnetic resonance spectroscopy (1H-MRS) study. MEG was obtained to 40-Hz amplitude-modulated stimuli. Spectral analyses in source space examined the phase locking and evoked power of the auditory steady state response (ASSR). 1H-MRS was obtained in the left auditory cortex using a 3T system using a MEGAPRESS j-editing sequence. GABA concentration, expressed relative to creatine, was correlated with the left hemisphere auditory responses obtained from MEG.

Significant positive correlations, after correction for multiple comparisons, were obtained between GABA and ASSR phase locking, both at the modulation frequency and for the first harmonic of the modulation at 80 Hz. We observed this correlation across the duration of the response, indicating that it was not restricted to the obligatory transient gamma-band response portion of the ASSR.

The relationship between ASSR and GABA suggests that some of the GABAergic inhibitory mechanisms proposed for gamma-band generation are applicable to driven auditory responses.

GAMMA OSCILLATIONS IN A THALAMOCORTICAL BINDING NETWORK EXPLAIN DEFICITS IN SPEECH-IN-NOISE UNDERSTANDING IN AGING

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Binding of auditory sensory information into an object, which then becomes accessible for perception and cognition, occurs through synchronous oscillations at gamma frequencies (40-80 Hz) in coupled thalamocortical networks. With MEG and auditory 40-Hz stimulation, we recorded simultaneously 40-Hz oscillations in a sensory circuit and a binding network. Both components of gamma oscillations were differently sensitive to informational masking, which allowed to separately analyze them. Comparing the temporal dynamics of gamma oscillations in a gap-detection task showed that sensory responses were comparable in young (mean age 25 years) and older (mean age 70 years) participants. However, binding related gamma oscillations were significantly reduced in the older participants. Moreover only the amplitudes of the binding gamma were correlated with participants' performance in speech-in-noise understanding but not the sensory response. The results are consistent with previous findings that in elderly people sensory information are encoded with high acuity at cortical level, however with advancing age it becomes increasingly difficult to interpret sensory information and make sense out of it. The results provided new insights into the role of thalamo-cortical gamma oscillations for sensory binding and into central mechanism of aging.

ENTRAINED THALAMO-CORTICAL NETWORKS IN FEAR CONDITIONING

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Despite a fair amount of knowledge on brain structures "active" during fear conditioning, the dynamic interplay within this network is still an active research topic. Via visual steady-state response (vSSR) in MEG we intended to uncover not only when certain regions are driven to a differential manner by the CS+ and CS-, but also map out the interaction pattern among these regions. Two fearful faces served as conditioned stimuli (CS) flickering at 15-Hz. An electrical stimulation on the left median nerve was the unconditioned stimulus (US) paired to the CS+. Time-frequency analysis revealed increased power during CS+ and source analysis indicated stronger responses also in limbic regions contralateral to the upcoming US. Entrained regions complementarily to the evoked power findings were indicated via coherence between brain activity and the "entraining signal". After identifying the major players in the fear conditioning network, a data-driven approach was followed to

investigate functional connectivity among these regions. This resulted in a distributed network, in which the thalamus contralateral to the upcoming US appears to act as a hub. Overall, our work sheds light on the spatiotemporal dynamics of regions involved in fear conditioning and illustrates the importance of thalamocortical connectivity in understanding this phenomenon.

MODULATION ENCODING IN AUDITORY CORTEX

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Amplitude modulation (AM) and frequency modulation (FM) are fundamental components of natural sounds, such as speech or music. We used MEG with its high temporal resolution and simultaneous access to multiple auditory cortical areas to show different types of modulation encoding in the human auditory cortex.

In the case of sinusoidally amplitude modulated carriers, we show that the modulation transfer functions are broadly lowpass in shape and roughly independent of bandwidth. When two modulation rates occur concurrently, the presence or absence of non-linear cross-terms are in accord with the psychophysical concept of modulation filterbanks. When dual modulations occur at nearby rates, they can induce cross-modulation-rate beating in analogy with the beating in cochlear filterbanks.

In the case of concurrent AM and FM modulations, we find non-linear modulation encoding: the neural modulations occur at the same rates as the acoustic modulations, but also at cross-modulation frequencies. When acoustic rates are substantially different, the combined modulation encoding appears at both modulation rates and additionally the faster neural modulation is modulated at the slower rate. This secondary modulation can be phase or amplitude modulation of the faster neural signal, or both, and we show examples of several different forms.

CONTINUOUS SPEECH ENTRAINS CORTICAL BRAIN OSCILLATIONS

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Cortical oscillations have been shown to be modulated during speech processing. Here, we monitored continuous speech processing with magnetoencephalography (MEG) to unravel the mechanisms of interactions between rhythmic components in speech and brain oscillations. We demonstrate that speech entrains the phase of low-frequency (delta, theta) and the amplitude of high-frequency (gamma) oscillations in the auditory cortex. Phase entrainment is stronger in the right and amplitude entrainment is stronger in the left auditory cortex. Furthermore, edges in the speech envelope phase reset auditory cortex oscillations thereby enhancing their entrainment to speech. This mechanism adapts to the changing physical features of the speech envelope and enables efficient, stimulus-specific speech sampling. Finally, we show that within the auditory cortex, coupling between delta, theta, and gamma oscillations increases following speech edges. Importantly, all couplings (i.e., brain-speech and also within the cortex) attenuate for backward-presented speech, suggesting top-down control. We conclude that segmentation and coding of speech relies on a nested hierarchy of entrained cortical oscillations.

SENSORIMOTOR OSCILLATIONS RELATED TO PREDICTIVE TIMING IN MUSICAL RHYTHM PROCESSING IN CHILDREN AND ADULTS

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When listening to rhythmic auditory patterns, people easily extract the timing regularity, predict the onset of the next beat, and synchronize body movements accordingly. We examined auditory-motor interaction and its relationship to neuromagnetic and neuroelectric beta oscillations.

When listening to the isochronous unaccented auditory beats of metronome clicks, the periodic beat structure as well as the musical meter such as a march or waltz can be induced by either prior finger tapping or listening to metrically accented patterns. Our MEG results show that this internalized timing processing is reflected in the temporal dynamics of beta-band oscillations.

With EEG recordings in adults and 7.5-year-old children during passive listening to isochronous tone sequences at three beat intervals of 390, 585, and 780 ms we demonstrate the feasibility of developmental studies in young children. The amplitude and latency of the beat induced beta desynchronization as well as the slope of the rebound were analyzed in relation to age and tempo. Both children and adults showed beta band desynchronization. Differences between age groups were most prominent at the fastest tempo. The results indicate that oscillatory networks can be investigated using EEG and that beta oscillations reflect rhythm encoding in children as well as adults.

DEVELOPMENT OF AUDITORY AND SENSORIMOTOR BRAIN RHYTHMS STUDIED WITH A CUSTOM-SIZED PEDIATRIC MEG SYSTEM

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We used a custom-sized MEG system optimized for pre-school aged children for studying developmental changes in brain activity during the crucial period between infancy and school age.

Developing a child-friendly experiment protocol accommodated the cognitive and attentional capacities and motivational requirements of 3 to 5 year old children. We report recent data on the auditory cortical temporal modulation transfer function in children and how this function differs from that of adults.

Moreover, we recorded mu, beta and gamma band activity during self-paced movements in 3 to 5 year old children, confirming that sensorimotor rhythms are present at an early age. The timing and frequency of oscillatory

activity differed from the typical adult pattern, including greater co-modulation of mu and beta activity at lower frequencies. Transient gamma bursts at movement onset were similar to that observed in adults, but occurred in both high and low gamma bands.

These novel findings indicate that basic sensorimotor rhythms are still undergoing maturational changes during preschool age, and may reflect organizational changes in sensorimotor networks. Such changes in have implications for both early brain development and our understanding of the role of this activity in normal and abnormal cognitive development.

S21: WHAT DISEASE TEACHES US ABOUT OSCILLATIONS AND VICE VERSA

CHAIRS:

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Oscillatory activity of the human brain has received growing interest as a key mechanism of large-scale integration across different brain regions. In addition, a crucial role of oscillatory activity has been postulated for the emergence of neurological and psychiatric diseases. MEG work played and plays an important role in quantifying and characterising changes of oscillatory activity and revealing their impact in disease.

In this symposium a closer look will be taken at four pathological entities and associated changes of oscillatory activity: movement disorders, stroke and recovery, multiple sclerosis, and hepatic encephalopathy. All of these diseases are good examples how studying oscillatory activity can ease unravelling pathophysiological mechanism, as various specific changes of neural oscillations have been described. These changes were observable in different frequency bands and networks of the brain. Vice versa, findings in these patient populations can help understanding the role of oscillatory activity in physiology, i.e. healthy subjects.

Taken together, this symposium aims to give an update on the translational use of MEG studying alterations of oscillatory activity in disease and how this can help understanding the functional role of oscillations.

OSCILLATORY BRAIN NETWORKS IN MOVEMENT DISORDERS: AN INSIGHT FROM COMBINED MEG AND INTRACRANIAL RECORDINGS

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Deep Brain Stimulation (DBS) surgery affords a unique opportunity to record local field potentials (LFP) from sub-cortical structures in awake humans. Combining such recordings with MEG makes it possible to characterise the oscillatory connectivity of DBS targets with the rest of the brain and look at modulation of oscillatory activity and connectivity by tasks and medication.

Our analysis of combined LFP-MEG recordings in Parkinson's Disease (PD) patients with electrodes in the subthalamic nucleus (STN) revealed two distinct resting oscillatory networks: a temporoparietal-brainstem network coherent with the STN in the alpha (7 - 13 Hz) band and a predominantly frontal network coherent in the beta (15 - 35 Hz) band. In addition, we found an increase in high-gamma (60-90 Hz) coherence between the STN and sensorimotor areas during movement with concurrent suppression of coherence in the alpha network. Both alpha and gamma effects were enhanced by dopamine and correlated with clinical improvement.

Our more recent results suggest that these networks are not an exclusive feature of STN and PD but are also present in other subcortical structures and other disorders. Our efforts to understand the role of these networks in health and disease will be the subject of my presentation.

MOTOR CORTEX OSCILLATIONS AND STROKE RECOVERY

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Electro- and magnetoencephalographic recordings of brain oscillations may reveal alterations in motor cortex functions. Reactivity of ~20-Hz oscillations to somatosensory stimulation has been shown to reflect motor cortex excitability. Coherence between motor cortex oscillations (in the ~20-Hz range) and electromyographic signals from the active muscle during isometric contraction is suggested to reflect cortical control.

In stroke, similar clinical symptoms, such as upper limb weakness, may result from different lesion types (cortical vs. subcortical), but their effect on cortical functions is likely to differ. In acute stroke patients, alterations in the reactivity of ~20-Hz oscillations have indicated that motor cortex excitability is increased in both hemispheres within the first week after stroke, and that the increase is negatively correlated with the dexterity of the impaired hand. This hyperexcitability gradually decreased within three months, in parallel with functional recovery. However, our recent results suggest that in acute stroke patients both the ~20-Hz reactivity and cortico-muscle coherence are affected differently by cortical and subcortical lesions. With MEG measurements of brain oscillations it may be possible to differentiate changes in motor cortex functions according to lesion type and thus to help to tailor individual therapeutic interventions, such as pharmacological manipulation or non-invasive brain stimulation.

OSCILLATIONS AND FUNCTIONAL BRAIN NETWORKS IN MULTIPLE SCLEROSIS

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Multiple Sclerosis (MS) is an inflammatory demyelinating and neurodegenerative disease leading to clinical and cognitive dysfunction to varying degree. Despite much progress in the MS field in recent years, there is a discrepancy between classical MRI findings such as white matter lesion load and clinical dysfunction. To bridge this gap we used MEG to assess oscillatory activity, functional connectivity and functional brain networks in MS. I will first demonstrate how pathological changes in oscillatory activity are associated to cognitive status in MS, i.e. relative power in the lower alpha (8-10Hz) band was negatively associated with cognitive status. Secondly, I will go one step further by analysing functional connectivity during the resting-state.

We found very consistently that across our studies there is a decrease in functional connectivity in the upper alpha (10-13Hz) band in MS patients. Thirdly, we analysed the topology of the functional networks that were formed by the functionally connected regions. Here, we used a so-called Minimum Spanning Tree (MST) analysis, which avoids potential biases that might arise due to differences in, for example, network densities.

THE SLOWED BRAIN: CORTICAL OSCILLATORY ACTIVITY IN HEPATIC ENCEPHALOPATHY

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This talk will present current MEG work studying oscillatory activity in patients suffering from hepatic encephalopathy (HE), a brain impairment due to reduced liver function. A slowing of the frequency of oscillatory activity was demonstrated for spontaneous brain activity, with respect to motor behaviour and motor symptoms, and in the context of visual attention processes and somatosensory processing. The observed slowing extends across different subsystems of the brain and has been confirmed across different frequency bands (alpha (8-12 Hz), beta (15-30 Hz), gamma (30-100 Hz)), providing evidence for ubiquitous changes of oscillatory activity in HE.

Interestingly, the so-called critical flicker frequency (CFF) as a simple measure of the processing of an oscillating visual stimulus has emerged as a useful tool to quantify HE disease severity, correlating with behavioural and neurophysiological alterations. Moreover, the CFF reliably distinguishes patients with clinical manifest HE from cirrhotics without any signs of HE and healthy controls using a cut-off frequency of 39Hz.

Although the underlying causal mechanisms are not yet understood, the presented results indicate that pathological changes of oscillatory activity play an important role in the pathophysiology of HE.

S22: REAL-TIME SIGNAL PROCESSING AND SOURCE LOCALIZATION FROM MEG MEASUREMENTS

CHAIRS:

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Providing high temporal resolution for non-invasive mapping of human brain functions, Magnetoencephalography (MEG) is optimal to monitor brain activity in real-time. In combination with up-to-date computational capacities, novel data processing and source imaging strategies are designed that provide results in real-time. Real-Time MEG feedback has shown the potential to advance basic and clinical research with respect to e.g. neurofeedback rehabilitation, novel paradigms adaptive to subjects' reactions and BCI. Reconstructing the measured signals to the source space allows for the reduction of noise and enhanced feature extraction which enables single trial brain analysis.

This symposium aims at collecting current developments and clinical applications in the fast evolving field of real-time signal processing and source localization from MEG measurements.

MEG NEUROFEEDBACK BASED ON ATTENTION MODULATION OF POSTERIOR ALPHA ACTIVITY

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Posterior alpha-band activity has been demonstrated to reveal low power in the hemisphere contralateral to the direction of attention, whereas the ipsilateral hemisphere exhibits relatively higher power. Crucially, the magnitude of lateralized posterior alpha power strongly correlates with the perception sensitivity. While recording MEG data we decoded the participants' direction of attention and presented the classification outcome online visually to the subject. In the first study, we investigated the feasibility of using posterior alpha power as an online control signal and its' trainability and robustness across sessions. In the second study, we investigated the behavioral consequences of covert attention neurofeedback training based on alpha lateralization. We found that only 10 minutes of neurofeedback training induced profound changes in perception sensitivity, while no effects were found in the control group. Surprisingly, the neurofeedback training in one hemifield resulted in deteriorated performance in a subsequent visual detection task in the untrained hemifield. No changes in perception sensitivity at the trained hemifield or in the control group were found. These studies show posterior alpha activity can be used as a control signal in an online setup and it can be trained. This training has consequences for the performance in an attention task.

RTMEG: A REAL-TIME SOFTWARE FOR RELAYING MEG SIGNALS

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To date, the majority of studies using magnetoencephalography (MEG) rely on off-line analysis of the spatiotemporal properties of brain activity. Real-time MEG feedback could potentially benefit multiple areas of basic and clinical research: brain-machine interfaces, neurofeedback rehabilitation of stroke and spinal cord injury, and new adaptive paradigm designs, among others. We have developed a software interface to stream MEG signals in real time from the 306-channel Elekta Neuromag MEG system to an external workstation. The signals can be accessed with a minimal delay (≤45 ms) when data are sampled at 1000 Hz, which is sufficient for most real-time studies. We also show here that real-time source imaging is possible by demonstrating real-time monitoring and feedback of alpha-band power fluctuations over parieto-occipital and frontal areas. The interface is made available to the academic community as an open-source resource.

EFFORTS FOR IMPROVING REAL-TIME CONTROLLABILITY OF MOTOR IMAGERY BRAIN COMPUTER INTERFACE – EEG AND SIMULTANEOUS MEG/EEG

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While brain computer interfaces (BCI) can be employed for humans, there are some problems remained to be solved prior to moving into market place. In most BCI systems, it is known that the significant number of target users are not able to use BCI systems with a control paradigm such as motor imagery (MI), P300, and steady state evoked potential (SSEP). Such target users are called the BCI illiterate users. Especially, in motor imagery BCI, a clear understanding of the BCI illiteracy mechanism or solution to this problem is lacking.

In this work, we briefly review the previous studies and summarize their findings about motor imagery in BCI. Further, we investigate both single modal EEG and multi-modal MEG/EEG data under the same motor imagery paradigm in order to seek neuro-physiological factors which are associated with motor imagery BCI performance. Various sensor-level and source-level analyses are applied on both numerous EEG and MEG/EEG data. We discuss how our findings may interpret real-time dynamical mechanism during MI, and propose the possible strategies to develop better real-time BCI systems.

A TOOLBOX FOR REAL-TIME NEUROELECTROMAGNETIC SOURCE IMAGING

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We developed a toolbox extending OpenWalnut which provides real-time processing of MEEG data up to reconstruction of distributed sources on the folded cortical surface. We followed a strictly modular concept, i.e. the signal processing chain is split into logical processing blocks, each of which is implemented as a unique parameterizable module with dedicated input and output links. This allows a flexible setup of the processing chain, e.g., branches in the signal flow to run different inverse algorithms can be created. Incoming data is collected at the input of each module and, after processing, passed to connected modules, and so forth. To achieve real-time requirements, we utilized NVIDIA's CUDA technology.

The currently available modules are: (1) data import module which is either a physical link to a Neuromag Vectorview System (Elekta, Finland) based on MNE software or a signal generator, (2) FIR filter, (3) epoch separation to extract event related responses, (4) epoch averaging, (5) source localization. For (5), the forward model has to be precomputed before the actual recording after the individual measurement setup is completed. We use leadfield interpolation as a time efficient solution. Real-time capabilities were tested in an experiment with somatosensory stimulation of the hands (weak electrical pulses).

MEG/EEG REAL-TIME ANALYSIS AND REAL-TIME SOURCE LOCALIZATION

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MEG and EEG are able to provide real-time information about subject's neural reactions, through e.g. real-time source localization. This allows the adaptation of stimulation paradigms during the measurement and creates a whole set of new experiments. A positive side effect of real-time processing is the shortened subsequent offline analysis.

We present our real-time MEG/EEG processing chain which provides real-time analysis in sensor and source space. Our source localization algorithm is based on gain matrix clustering and can deal with low SNR data. We obtain a localization rate of about 100 per second. A closed feedback loop for stimulations based on source localization results is realized with a delay of 6ms.

Real-time analysis and stimulus generation are realized with the recently introduced MNE-X acquisition software. This software package provides a highly scalable plugin system which can be easily extended. A MNE-X trigger box in combination with a MNE-X trigger plugin was designed to provide real-time adapted stimulations.

S23: IMPACT INVESTIGATION OF MEG AS DIRECT DIAGNOSTIC METHODS

CHAIR:

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MEG is one of the most powerful diagnostic tools for neurological disorders.

Since MEG can demonstrate evident and clear findings on cerebral cortex non-invasively, the application is emphasized for the disease in childhood.

Here, we would like to introduce the striking evidence for understanding neurological disorders in childhood.

ANGELMAN SYNDROME

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Angelman syndrome (AS) is thought to be one of the few neurodevelopmental disorders with GABAergic-related genetic involvement. AS results from a functional deficit of the imprinted UBE3A gene in 15q11-q13, resulting mainly from a 4-Mb deletion that includes GABAA receptor subunit genes. To understand the underlying cortical dysfunction, we have investigated the primary somatosensory-evoked responses in AS patients. Subjects included eleven AS patients with a 15q11-q13 deletion (AS Del), two AS patients without a 15q11-q13 deletion, but with a UBE3A mutation (AS non-Del), six epilepsy patients (non-AS) and eleven normal control subjects. Somatosensory evoked fields (SEFs) in response to median nerve

stimulation were measured by magnetoencephalography. The N1m peak latency in AS Del patients was significantly longer than that in non-AS patients or normal control subjects. The next component, P1m, was prolonged and ambiguous, and was only detected in patients taking clonazepam. In contrast, SEF waveforms of AS non-Del patients were similar to that of control individuals, rather than to AS Del patients. Thus, GABAergic dysfunction in AS Del patients is likely due to hemizygosity of GABAA receptor subunit genes, suggesting that GABAergic inhibition plays an important role in synchronous activity of human sensory cortex.

FOCAL CORTICAL DYSPLASIA

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Objective: To evaluate whether dynamic statistical parametric mapping (dSPM) could delineate characteristic epileptiform of FCD and its underlying network.

Methods: We retrospectively studied 80 epileptic spikes from 10 children with symptomatic localization-related epilepsy by using dSPM. FCD group consists of five patients with FCD diagnosed by MRI including one case with pathological confirmation of FCD typeIIA. Non-FCD group consists of hippocampus sclerosis, cavernous hemangioma, and non-lesion.

We compared spatiotemporal activity between both group by demonstrating morphology and temporal activity of each spike. Spike power was represented by Z score, a statistical significance from the back ground.

Results: Epileptic spike in FCD group was (1) Spike activation emerged and diminished rapidly in same location without extending to adjacent lobes (2) Z score was larger than non-FCD group ($p<0.01$), (2) steep and single in spike morphology ($p<0.01$) . In contrast, non-FCD group showed (1) rather extended spike volume that spread to multiple cortex and diminished slowly toward different lobe (2) multiple and moderate shape in morphology. dSPM also delineate spike activity of MRI invisible case.

Significance: Our study shows dSPM can demonstrate characteristic feature of epileptic spikes of FCD as well as its underlying network with spatiotemporal resolution.

ATYPICAL BENIGN PARTIAL EPILEPSY IN CHILDHOOD (ABPE)

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Rationale: Atypical benign partial epilepsy (ABPE) is characterized by centro-temporal electroencephalography spikes, continuous spike and waves during sleep (CSWS), and multiple seizure types including epileptic negative myoclonus (ENM), but not tonic seizures. This study evaluated the localization of magnetoencephalography (MEG) spike sources (MEGSSs) to investigate the clinical features and mechanism underlying ABPE.

Methods: We retrospectively analyzed seizure profiles, scalp video EEG (VEEG), and MEG in ABPE patients.

Results: Eighteen ABPE patients were identified. Initial seizures consisted of focal motor seizures (15 patients) and absences/atypical absences (3). VEEG showed centro-temporal spikes and CSWS in all patients. Magnetic resonance imaging (MRI) was reported as normal in all patients. MEGSSs were localized over the following regions: both Rolandic-sylvian (8), perisylvian (5), peri-Rolandic (4), parieto-occipital (1), bilateral (10), and unilateral (8). All patients were on more than two antiepileptic medications. ENM and absences/atypical absences were controlled in 14 patients treated with adjunctive ethosuximide.

Conclusion: MEG localized the source of centro-temporal spikes and CSWS in the Rolandic-sylvian regions. Centro-temporal spikes, Rolandic-sylvian spike sources, and focal motor seizures are evidence that ABPE presents with Rolandic-sylvian onset seizures.

SCHIZOPHRENIA AND AUTISM SPECTRUM DISORDER

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Schizophrenia is a mental disorder characterized by a breakdown of thought processes and by a deficit of typical emotional responses. Common symptoms include auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking, and it is accompanied by significant social or occupational dysfunction. The onset of symptoms typically occurs in young adulthood. On the other hand, autism spectrum disorder (ASD) is a disorder of neural development characterized by impaired social interaction and verbal and non-verbal communication, and by restricted, repetitive or stereotyped behavior. These symptoms typically become apparent before three years old.

In 1970s, Feinberg predicted deficit in efference copy and/or corollary discharge played role in symptoms of patients with schizophrenia. Recent neurophysiological approach proved dysfunction of gating deficit in schizophrenia more clearly.

Recently, Rapoport reported child onset schizophrenia is preceded by and comorbid with ASD in 30%-50% of cases and epidemiologic and family studies find association between the disorders. We conducted to investigate gating deficit in schizophrenia using somatosensory evoked fields by using self-generated stimulation and externally-generated stimulation. Our results suggested similar findings in both schizophrenia and ASD compared to control group, which suggests these two disorders may have a shared neuropathology.

Posters

P1-001

A DISCONTINUOUS GALERKIN FINITE ELEMENT APPROACH FOR THE EEG FORWARD PROBLEM

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The accuracy of the inverse problem in source analysis strongly depends on the accuracy of the forward problem. For the forward problem, numerical approaches are needed to compute head surface field distributions from dipolar current sources using realistic head volume conductor models. Here, to the best of our knowledge, we have for the first time evaluated a Discontinuous Galerkin Finite Element Method (DG-FEM) for the EEG forward problem. We will start with the basic mathematical framework for the DG-FEM approach when using the FE subtraction method for modelling the singularity arising from the choice of a mathematical current dipole as a source term. The new approach was implemented in the DUNE framework (http://www.dune-project.org), a modular C++ toolbox for solving partial differential equations using grid-based methods, a free and open-source software. For validation purposes, results of our implementation will be presented in an accuracy study using tetrahedral and hexahedral FE models with different resolutions of multi-layer sphere models where quasi-analytical solutions exist. We will show that our DG-FEM implementation achieves very high accuracies even for the most eccentric sources, whose distance to the next conductivity jump is less than a millimeter. It will also be shown that, especially for eccentric sources, higher order basis functions can be used to further strongly increase numerical accuracy. Finally, we will present a visualization of DG-FEM simulation results performed in a realistic six-compartment (skin, skull compacta, skull spongiosa, cerebrospinal fluid, brain grey and anisotropic white matter) head model.

P1-002

MNE FOR MEG AND EEG DATA PROCESSING: WHAT'S UP?

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MNE is a software package for processing magnetoencephalography (MEG) and electroencephalography (EEG) data. It provides a full workflow for data preprocessing, automatic forward modeling (with FreeSurfer) using boundary element models (BEM), source imaging using distributed source models, time-frequency analysis, non-parametric statistics, and connectivity measures, in both sensor and source space. MNE is developed by an international team of contributors, with particular care on computational efficiency, code correctness and readability, enabling reproducibility of results. The core of MNE, available for Linux and Mac OSX, consists of command line tools and two graphical user interface applications. MNE-Python adds powerful scripting capabilities to the MNE stack while being 100% compatible with existing MNE tools and commercial Neuromag software. MNE-Python heavily utilizes the Neuromag FIF file format for data storage (raw, epochs, ERF/ERP, ICA, SSP, forward, inverse etc.), but recently more readers of raw data have been added (4D BTI, KIT, Brainvision, EDF/BDF). MNE-Python supports source imaging with Minimum Norm Estimates (MNE), dSPM, sLORETA, LCMV Beamformer, and (Time-Frequency) Mixed-Norm Estimates ([TF]MxNE). Moreover, support for Gamma-MAP (a sparse Bayesian learning based inverse solver) and TF beamformers (DICS, 5d) was added. Some features were recently improved such as time/frequency-domain analysis, non-parametric statistics (addition of TFCE method), and artifact correction with ICA (a decomposition on a 40 min. run of MEG data can be performed in 2..3 minutes on a modern laptop). Other recent additions are: decoding/MVPA capabilities, realtime analysis, forward modeling, and data projection onto virtual sensors for field interpolation. An up to date list of changes is available online. As a complement to the MNE sample dataset, MNE now gives easy access to the SPM demo data on faces. In 12 months, MNE-Python has almost doubled its number of core contributors and number of lines of code.

P1-003

A TOOLBOX FOR REAL-TIME NEUROELECTROMAGNETIC SOURCE LOCALIZATION

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EEG and MEG provide insight into neuronal processes in the brain on a real-time scale. To exploit the advantage of a high time resolution, online analysis of such signals is particularly interesting. We developed software, which principally allows online processing and visualization of brain activity in real-time. According to our best knowledge, the toolbox is conceptually different from other solutions which provide online processing capabilities - we aim to provide source localization using a high density source space (more than 250.000 sources) from high channel EEG/MEG data. Furthermore, the signal flow is easily set up by using graphical building blocks.

Our toolbox NA-Online1 is based on OpenWalnut, which is extended by the following modules: (1) data import modules, a physical link to a Neuromag Vectorview System (Elekta, Finland) based on MNE software, a reader for FIFF file format a. m., (2) alignment between Fiducial/AC-PC coordinates, (3) EEG leadfield interpolation, (4) FIR filter, (5) epoch separation, (6) epoch averaging, (7) source localization. For (5), the forward model has to be precomputed before the actual recording after the individual measurement setup is

completed. We use (3) as a time efficient solution. Real-time capabilities are achieved by using modern high performance computing technology, i. e. graphic processing units with NVIDIA CUDA.

We practically applied the software for online localization of evoked brain activity in the primary motor cortex. Current developments to account for head movements will also provide imaging based on MEG data. A connection to the FieldTrip Buffer2 will provide access to other signal acquisition systems. While we proofed our concept for online processing based on time domain analysis, future development will certainly also include processing in the frequency domain. Besides source imaging, other fields of application can be found in neurofeedback and BCI systems.

1 https://bitbucket.org/labp/na-online_ow-toolbox
2 http://fieldtrip.fcdonders.nl/development/realtime

P1-004
MEGA_STATS: A STATISTICAL TOOLBOX FOR MEG, EEG & INTRACEREBRAL EEG DATA ANALYSIS

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We present MEGA_STATS a software toolbox for statistical analysis of MEG, EEG and intracerebral EEG data based on the cross-platform Matlab environment (The Mathworks, Inc.). The toolbox is developed at the MEG-EEG center at CENIR, Paris (CENIR: http://meg.cenir.org).

MEGA_STATS can be used to compute statistics on electro- and magneto-encephalographic signals. The toolbox accepts multiple input format (CTF, ELekta, Matlab …).

It allows the analysis at

- sensor level,
- the neural source level,
- time sample level,
- single and multiple trials level,
- time-frequency level.

The user specifies his design in a Matlab script. This design can be of any number of independent factors, each with multiple levels, with repeated measurements or between groups.

The available statistical analysis methods include parametric and non parametric testing, one way and multi-factors analysis of variance for within subjects and between groups. It includes also paired and unpaired t-test for single factors with two levels.

The output files contain F, t, p or -logp values for every main effect and interaction.

Additionally, the user has the ability to control for multiple comparison using the cluster-based permutation proposed by E.Maris & collaborators. This algorithm was extended to multiple factors and multi levels repeated measures as well as between groups and between trials analysis of variance. It computes the corrected p values for each factor as well as for interaction based on Monte Carlo permutation test.

The suite is open-source, implemented in C/C++/Matlab (available under Linux / Mac OSX / Windows), and can be downloaded at http://meg.cenir.org.

E.Maris et al J. Neurosci. Methods, 164, 177–190

P1-005
ANYWAVE: A SOFTWARE FOR VISUALIZING AND PROCESSING ELECTROPHYSIOLOGICAL SIGNALS

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Introduction: The importance of digital signal processing in clinical neurophysiology is growing steadily. Two communities are involved: researchers in clinical neuroscience on the one hand and methodologists developing signal processing algorithms on the other hand. Therefore, there is a need for crossing the gap between these communities by providing software that permits a fast use of newly designed algorithms.

Our goal was to develop software which would both visualize and process signals on the one hand and act as a software development platform to add existing or new signal processing algorithms on the other hand.

Features: AnyWave was designed to run efficiently on several computer platforms and is written in C++ using the Qt's framework. It provides access to a variety of data formats, and permits a sharp visualization of signals with an anti-alisiasing procedure.

AnyWave allows including external processing tools as plug-ins, which can be developed in an easy and efficient manner in different languages including Matlab and Python. In the current version, Anywave implements computation of connectivity graphs (non-linear correlation h2) and time-frequency representation.

The software is freely available at http://meg.univ-amu.fr under the LGPL3 license.

Conclusion: We propose AnyWave as an efficient EEG-MEG reader with fast evolution capabilities. In contrast with existing solutions, AnyWave offers an interface that suits the needs of clinical research with the possibility of easily adding signal processing plug-ins. With this software, we expect to strengthen the collaboration between clinical neurophysiologists and researchers in biomedical engineering and signal processing.

P1-006
WEBMEG: AN INTERACTIVE WEB-BASED TOOL FOR THE VISUALIZATION AND ANALYSIS OF MEG AND EEG DATA

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The analysis of magnetoencephalography (MEG) and electroencephalography (EEG) data requires high technical expertise and is frequently performed by either using relatively expensive commercial or open-source academic software tools predominantly written in MATLAB. With very few exceptions, the use of most of these softwares requires intermediate knowledge of computer programming. This requirement limits the widespread use of these neuroimaging techniques to users who have the necessary technical skills. Here, we have developed an interactive web-based software, called WebMEG (http://www.webmeg.net), for the analysis of EEG and MEG data. WebMEG is designed using HTML5, JavaScript and Cascading style sheets (CSS). It incorporates external libraries such as Highcharts and Apycom for providing a fluid visualization experience. File parsers were developed in JavaScript for reading the binary EEG/MEG data. The software allows one to navigate across the raw data, exclude bad channels, filter (notch, low-pass, high-pass), create and save custom EEG channel montages, mark physiological or pathological (i.e. interictal spikes) events, map activity on head topography, and average across trials. Functions to detect TTL pulses for automatic trigger detection and detection of epileptic interictal spikes have also been implemented. The users can load/save the marked trigger or spikes events for future use or share for collaborative purposes. The software allows also the statistical analysis of data at the sensor level by using paired t-test and analysis of variance across experimental conditions. Functionality to load/save macros is available that enables the users to save her/his work once the browser is closed. Being a completely client-side software and without the requirements of any outgoing data transfer, WebMEG ensures the patient privacy according to the Health Insurance Portability and Accountability Act (HIPPA). The functionalities are currently restricted to analysis at the sensor level. Future developments will include visualization of the anatomy and scripts to perform source analysis.

P1-007
[MEG]PLS: A PIPELINE FOR MEG DATA ANALYSIS AND PLS STATISTICS.

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The emphasis of modern neurobiological theories has recently shifted from the independent function of brain areas to their interactions in the context of whole-brain networks. As a result, neuroimaging methods and analyses have also increasingly focused on network discovery. Magnetoencephalography (MEG) is a unique neuroimaging modality in the sense that it captures neural activity with a high degree of spatial and temporal specificity, providing detailed, time varying maps of neural activity and interactions. Partial least-squares (PLS) analysis is a multivariate framework that can be used to isolate distributed spatiotemporal patterns of neural activity that differentiate groups or cognitive tasks, to relate neural activity to behaviour, and to capture large-scale network interactions. Here we introduce [MEG]PLS, a MATLAB-based platform that streamlines MEG data preprocessing, source reconstruction and PLS analysis in a single unified framework. [MEG]PLS facilitates MRI processing, including segmentation and coregistration, MEG preprocessing, including epoching, filtering and artifact correction, MEG source analysis, including multiple head models and beamforming algorithms, and combines these with a suite of PLS analyses. The pipeline is open-source and modular, utilizing functions from FieldTrip (Donders, NL), AFNI (NIMH, MD) and SPM8 (UCL, UK), which are extensively supported and continually developed by their respective communities. [MEG]PLS is flexible, providing both a graphical user interface and command-line options, depending on the needs of the user. A visualization suite allows multiple types of data and analyses to be displayed and includes 4D montage functionality and overlays of multiple analyses. We demonstrate the applicability of [MEG]PLS using sample MEG data from a cognitive learning experiment. [MEG]PLS is freely available under the GNU public license (http://meg-pls.weebly.com).

P1-008
OPEN-SOURCE MEG/EEG ACQUISITION SOFTWARE

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We developed MEG acquisition software employing a combination of the LabVIEW and Qt platforms. This software takes advantage of multiple features from LabVIEW such as queued state machine, powerful hardware access, multiple threads, parallel processing, and the convenient graphical programming. Our software also benefits from the features of Qt such as rich functional support, cross-platform compiler, and the flexible and powerful user interface. We connected the LabVIEW and Qt components by TCP/IP socket communication. Here, we will introduce the details of this architecture and describe the validation of the acquisition software in acquisition of data from our novel "BabyMEG" infant MEG system. Our results indicate that this software is able to acquire data consistently in real time, enabling a fast acquisition up to 5KHz with online display of both raw data and event-related averages. Thanks to its modular structure, our software can be easily extended with other real-time functions and can be adapted to other types of MEG and EEG hardware.

P1-009

SIMULTANEOUS MATCHING PURSUIT DECOMPOSITION OF EVOKED BRAIN RESPONSES IN M/EEG USING SPATIO-TEMPORAL DICTIONARIES

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We present a novel approach to a synergistic decomposition of evoked brain responses acquired by two electromagnetic modalities, i.e. magnetoencephalography (MEG) and electroencephalography (EEG), aiming at a sparse representation of the underlying brain activity in terms of spatio-temporal atoms. The introduced algorithm is based on the Multivariate Matching Pursuit (MMP) algorithm. We name it Spatio-Temporal Matching Pursuit (STMP), since it allows addressing spatial and temporal aspects of the analysed multivariate signal simultaneously. Spatio-temporal atoms can be readily interpreted physiologically, since localized source loci and corresponding waveforms can be unequivocally allocated to each other. STMP is able to separate different activities, resulting in source-specific waveforms, as one spatio-temporal atom reflects the activation of exactly one dipolar source. Our approach is also free from severe a priori assumptions about the solution space, thus allowing to avoid intricate inverse solutions. STMP is a source localization strategy free of setting any regularization parameters, in contrast to, e.g., previous MMP preprocessing approaches, where decomposing a signal containing contributions of temporally related but not identical activities yields one waveform addressing several processes.

Furthermore, we propose an optimization technique which enormously reduce the overwhelming computational cost by making use of the Cauchy-Schwarz inequality.

We demonstrate the efficiency of the STMP approach using an MEG data set obtained from a subject who was exposed to a simple auditory stimulus. We focused in the analysis on the most prominent late auditory evoked magnetic field, the M100 component. We assess the robustness of the performance for several signal-to-noise ratios using a permutation test on various subsets of trials.

P1-010

REAL TIME OCULAR AND CARDIAC ARTIFACT REDUCTION IN MEG

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Recently, magnetoencephalography (MEG) based real-time brain computing interfaces (BCI) have been developed to enable novel and promising methods for neuroscience research. It is well known that artifact rejection prior to source localization largely enhances the localization accuracy. However, many BCI approaches neglect real-time artifact removal due to its time consuming process.

Here an approach is introduced, which is capable of real-time ocular and cardiac artifact rejection. The method (referred to as ocular and cardiac artifact rejection for real-time analysis, OCARTA) is based on constrained independent component analysis (cICA), where a priori information of the underlying source signals is added in form of source specific cost-functions [1]. In OCARTA three different cost-functions are implemented: one for cardiac, one for ocular and another one for other biological activity. Thereby the subject's individual cumulative density functions of the cardiac and the ocular activity served as the internal cost-function for cardiac and ocular sources, respectively. For other biological sources the sigmoidal function is used since it is known to separate for many types of biological sources. As a result, the signal decomposition is performed fast and optimal with respect to the subject's individual cardiac and ocular activity.

OCARTA was tested and applied to data from three different but most common used MEG systems (4D-Neuroimaging, VSM MedTech Inc. and Elekta Neuromag). Ocular and cardiac artifacts were effectively reduced within one iteration and a time delay of 1 ms estimated on a standard PC (Intel Core i5-2410M), i.e. the algorithm offers real-time capability.

[1] Breuer et al., 2014, "A Constrained ICA Approach for Real-Time Cardiac Artifact Rejection in Magnetoencephalography"

Keywords: Ocular and Cardiac Artifact Rejection for Real-Time Analysis (OCARTA), Real-Time Artifact Reduction, Independent Component Analysis (ICA), Constrained ICA (cICA)

P1-011

VISUAL GAMMA OSCILLATIONS RECORDED WITH MEG ARE NOT AFFECTED BY THE MICROSACCADIC SPIKE ARTEFACT.

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Visual gamma oscillations (VGOs) are an important neural substrate of information processing and perception. However, EEG recordings of VGOs might be affected by the extra-ocular muscle artefact concomitant with miniature fixational eye movements called micro-saccades (Yuval-Greenberg et al., 2008). This is because the spectral bandwidths of the two activities overlap and because temporal distribution and other characteristics of micro-saccades are modulated by sensory stimulation. MEG, on the other hand, has been shown to be less contaminated by the artefact and thus MEG VGOs might not be affected at all. In order to test this, we recorded MEG simultaneously with remote high-speed video eye tracking while participants fixated on a central spot and were presented repeatedly with a high-contrast vertical grating (Muthukumaraswamy & Singh, 2013). In 14 subjects we detected a total of 6178 micro-saccades whose parameters were the same as those reported in less challenging environments (Engbert & Mergenthaler,

2006). At micro-saccade onset we observed the micro-saccadic spike artefact - a transient increase in broadband gamma power that had a predominantly temporal and frontal topography. Stimulus-locked activity localized with a beamformer revealed strong induced VGOs in an occipital source. Importantly, while at temporal sensors we observed on average higher gamma power around micro-saccade onsets than around randomly sampled time points, there was no difference between the two in the occipital source. In addition, there was no apparent relationship between the time course of VGO amplitude and the temporal distribution of micro-saccades. For instance, at ~ 150 ms after stimulus onset, at peak VGOs amplitude, we observed an almost complete suppression of micro-saccades. Moreover, no correlation was found between the micro-saccadic rate of occurrence and VGO amplitude or frequency. Our results provide direct evidence against MEG induced visual gamma oscillations being substantially affected, or even generated, by the micro-saccadic spike artefact.

P1-012

APPLICATION OF REAL-TIME ROBUST SIGNAL SPACE SEPARATION TO BABYMEG SYSTEM

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The recently proposed robust signal space separation (rSSS) method can be applied in real time and is very effective in suppressing environmental and biological noise from multichannel MEG data. We applied the rSSS method in real time to the data acquired from the babyMEG system that consists of two layers of magnetometers. The inner layer consists of 270 magnetometers and the outer layer of 35 triaxial magnetometers placed 4 cm above the inner layer. We applied the rSSS method to simulated MEG signals with consideration of three sources. The first source comprises 100 current dipoles randomly placed on a sphere inside a dewar to simulate brain activity. The second is a magnetic dipole placed 7 meters away from the sphere center to simulate environmental magnetic noise. The third is a channel noise imposed on an inner layer magnetometer to simulate a malfunctioning channel. The rSSS method suppressed the artifacts of the bad channel and the magnetic noise, and outperformed the conventional SSS in reconstructing the brain signals. Moreover, the real-time rSSS approach using both the inner and outer layer magnetometers was more effective in eliminating noise and was more robust than the same method using the inner layer sensors only.

P1-013

AN AUTOMATIC ALGORITHM FOR FINDING AND CLEANING CONTAMINATED MEG AND EEG CHANNELS

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Magnetoencephalography (MEG) and electroencephalography (EEG) are well-established, non-invasive, functional imaging modalities for measuring brain activity with excellent temporal resolution. They detect the activity by measuring the magnetic fields outside the head (MEG) or the electric fields at the scalp (EEG) that are generated by post-synaptic currents. Both MEG and EEG measure signals simultaneously from multiple sensors at different locations with respect to the brain.

However, both MEG and EEG measurements may include sensors that are contaminated by noise and artifacts. Often these channels are identified heuristically and completely removed from the analysis. We studied how noisy channels can be detected robustly and automatically, without heuristic information, and how we can simultaneously clean the channels. Additionally, we show how we can utilize the information even from the contaminated channels in an optimal way, without completely rejecting them.

We introduce a novel method for quantifying the qualities of MEG and EEG channels. The iterative algorithm uses a Bayesian approach to evaluate the reliability of each channel by taking advantage of the mutual information between different sensors. After the quality of each channel has been evaluated, we can emphasize less contaminated channels in the source localization. The improved source estimates are used to correct the contaminated channels.

Our simulations and results from real datasets show that the presented algorithm is able to quantify reliably the level of contamination in different sensors. Furthermore, the algorithm is effective in removing noise.

P1-014

SSS-BASED MOVEMENT COMPENSATION AND VIRTUAL HEAD-POSITION RELOCATION IMPROVE SENSOR-LEVEL ICA

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Head movement within the MEG helmet (and hence within the sensor array) presents a problem for sensor-level analyses of both individual and multi-subject data. Continuous head-position indicators (cHPI) allow for the HP to be estimated at regular intervals during the recording, and for movement compensation (MC) and HP transformation (HPTrans) to be applied offline by signal space separation (SSS; Taulu et al., 2005). MC in turn should enable source-separation methods

like independent component analysis (ICA) which assume that sources are static. We evaluated the efficacy of MC and HPTrans in SSS using the percent of variance (of VEOG) accounted for (PVAF) of the eye-blink-related ICA component(s). If MC-SSS and HPTrans adequately control for head movements within and between runs, the static-source assumption of ICA should be met, and the blink-IC PVAF should be higher than for non-MC or non-HPTrans SSS data. Data from 306 MEG sensors (102 magnetometers and planar gradiometer pairs) were recorded during a visual lexical decision task (two ~8-minute runs; N=18 adults). Temporal SSS was used to remove external noise, apply MC within runs, and apply HPTrans across runs/participants. ICA was run on all 306 sensors across two concatenated blocks for each participant. Each component's activation was correlated with VEOG signal, and the PVAF of the highest-correlated IC(s) measured. Blink IC PVAF was higher with MC-SSS than with non-MC SSS. When the second run HP was systematically incrementally misaligned to the first run using HPTrans, blink IC PVAF declined until a threshold was reached, at which point the blink was split across two components. When two participants' data were temporally concatenated, HPTrans to a common origin within the helmet enabled the extraction of a common blink IC, which was not always possible otherwise. MC and HPTrans with SSS improved ICA results both within and across subjects.

P1-015

REMOVING POWER LINE ARTIFACT WITH NO EXTERNAL CUE

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Power line artifact of 50 or 60Hz can interfere with MEG signal processing in the gamma frequency band. Using a notch filter removes the artifact, but also any brain signal at this frequency. It has been shown (Tal & Abeles, 2013) that recording the zero crossing of power line oscillations can serve as an external cue for time-locked averaging of mains artifact. The averaged artifact template can then be removed from each channel and each power line cycle, thus creating data free of power line artifact while preserving the brain signal in the same frequency. However, this procedure requires a special device for recording the timing of mains cycles. The current work suggests two methods for cleaning MEG data without an external cue. Power line cycles can be either detected using noise sensitive channels, such as MEG reference channels, or constructed artificially based only on the sampling rate and the power line frequency. Using data from different MEG sites, we show that the power line artifact can be successfully removed from the data using both methods. Although detecting the actual cycles in the MEG data leads to more efficient artifact removal, artificially constructing the cycles can also be sufficient and does not depend on the existence of noise sensitive channels. An open-code matlab toolbox with the cleaning method is available online. The toolbox can be used to remove power line artifacts from MEG or EEG data from any source. In addition to power line cleaning, the algorithm can be implemented to remove heartbeat artifact with a similar technique, reducing an averaged heartbeat template from each heartbeat instance in the data. Examples showing the advantages of the suggested cleaning procedures are given and discussed.

P1-016

RISING ABOVE THE NOISE: THE CHALLENGE OF COMBINING TDCS & MEG

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Transcranial Direct Current Stimulation (tDCS) is a neuromodulation technique capable of producing prolonged, polarity-specific alterations in cortical excitability [1]. Although the resulting changes are largely thought to reflect fluctuations in the excitation/inhibition balance, the physiological principles underlying the influence of tDCS are not completely understood. By applying DC stimulation during the acquisition of MEG data, the neurobiological effects of tDCS can be directly measured. The implementation of concurrent tDCS-MEG is at a preliminary stage, where detrimental factors such as the occurrence of magnetic artefacts, produced by the external electric field, are not well appreciated. The focus of the current study was to ascertain the extent and influence of such artefacts.

A 275 channel whole head CTF system was used to acquire neuromagnetic data relating to noise levels induced by the tDCS equipment, which formed the basis of the generated power spectra (dB/Hz). An initial investigation of noise as an average across all sensors demonstrated the presence of high amplitude artefacts, particularly at frequencies below 15Hz, during active and sham stimulation compared to the baseline recording. At the level of individual sensors, excess noise was present at locations local to and distant from the active electrode. However, the relative stability of power spectra following the removal of trials corresponding to the transient current onset and offset phases indicated that data acquisition is unlikely to be as compromised during the DC plateau. This highlights the potential for concurrent tDCS-MEG studies to generate sufficiently clean data from which accurate source localization estimates can be obtained, particularly if the SAM beamformer approach is adopted [2].

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P1-017

REMOVAL OF LARGE INTERFERENCES IN MEG SOURCE IMAGING BY POOR MAN'S TSSS

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This paper proposes a simple but efficient method to remove interference magnetic fields in MEG source imaging. The principle of the method is similar to that of the spatiotemporal signal space separation method (tSSS)[1]. The key difference is that the proposed method does not use vector spherical harmonic expansions. Instead, it makes use of the span of source-space

lead field. The method first estimates the orthonormal spatial basis vectors by applying the singular-value decomposition to the source-space lead field matrix, or equivalently, by applying the eigenvalue decomposition to the corresponding gram matrix. The eigenvectors associated with distinctively large eigenvalues are chosen, and the spatio-temporal MEG data containing interferences is projected onto the inside and outside the span of these eigenvectors. Let us define the projected data as Bin and Bout, and the subspaces spanned by the temporal singular vectors of Bin and Bout as Sin and Sout. The proposed method finds the intersection of Sin and Sout. The orthonormal basis set of the intersection is obtained as the principal vectors between Sin and Sout whose principal angles are equal to zero[2]. Since this intersection represents the interference subspace, the method projects the original MEG data onto the subspace orthogonal to the intersection. We show the method effectiveness by applying it to data from a patient with a vagus nerve stimulator and to speech-affected auditory data. Compared to the original tSSS, the implementation of the proposed method is much easier, because it does not use "expensive" vector spherical harmonic expansions. The method, therefore, may be called "the poor man's tSSS".

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P1-018

REGULARIZED HEAD POSITION TRANSFORMATION FOR MEG

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A particular challenge in pediatric magnetoencephalography (MEG) measurements is the difficulty of children to remain still during the measurement, sometimes compromising the quality of data. Continuous head position tracking and compensation algorithms have solved the problem in many cases. However, the sensor-level movement correction methods are based on data decomposition and reconstruction, which typically causes increased reconstruction noise with large head movements.

To decrease the reconstruction noise related to large head movements, we present an experimental regularization method for head movement correction based on signal space separation (SSS). Regularization is obtained by reducing the SSS model complexity at distant head positions with the criterion of maintaining the condition number of the SSS basis at the same level as that of the standard head position. Consequently, the head position transformation becomes numerically more stable and does not amplify noise components. Moreover, as the suppression of external magnetic fields by SSS is sensitive to inaccuracies of the calibration and geometry of the MEG device, improved stability of large head position transformations should help in maintaining the level of shielding against external magnetic fields.

Simulations with realistic signal-to-noise ratio show that the regularization does not introduce bias to the source localization. However, it decreases the reconstruction noise level considerably, to a level that allows robust head transformation distance to increase by several centimeters. Phantom data support these findings and also give evidence that the shielding factor of SSS remains stable with regularization when the transformation length increases.

The method potentially broadens the application of SSS-based movement correction by resulting in reliable data quality even to cases with large head movements and could be particularly useful in pediatric magnetoencephalography.

P1-019

BEAMFORMER ANALYSIS IS AUGMENTED WITH INDEPENDENT COMPONENT ANALYSIS SOURCE SUBSPACE REGULARIZATION

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The fundamental problem of source analysis with magnetoencephalography (MEG) lies in solving the inverse problem. One solution to this problem is the use of adaptive spatial filters that estimate source activity at each voxel by minimizing the contribution from all other voxels, such as beamforming. This approach suffers from the tendency of stronger dominant sources to mask weaker sources. A well-established technique to remove unwanted artefacts is Independent Component Analysis. In order to use ICA and beamformers simultaneously, however, regularization must be employed to ensure full rank of the covariance matrix. Using the smallest non-zero eigenvalue of the covariance matrix as the regularization parameter has been previously shown to improve the localization of frontal and temporal medial sources in the presence of ocular artefacts in adults. This regularization procedure requires addition of noise to all eigenvalues of the covariance matrix. Here, we added noise equivalent to the smallest non-zero eigenvalue to only those components that were removed. The covariance matrix was then computed and the beamformer weights were generated. Noise was not added to the data itself ensuring that the original signal to noise ratio was intact. This more restricted regularization also theoretically results in better resolution. We evaluated this technique in a working memory task for typically developing children (n=20, mean age 11.25 years) where there are often more event-related eye artefacts than seen in adults. Our approach recovered expected hippocampal activity 375-425 ms post stimulus onset (as when no ICA was applied), whereas with the previous regularization strategy this peak shifted 5mm laterally to the inferior temporal gyrus. Furthermore, the signal to noise ratio of peaks common between strategies increased, and peaks that had been obscured by excessive regularization were identified. We thus recommend this method be used when using ICA with beamformer based source analysis.

P1-020

COMPARISON OF EEG AND MEG COHERENCE FUNCTIONS BETWEEN A BRAIN SIGNAL AND A SOUND ENVELOPE IN A SELECTIVE LISTENING STUDY

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Objectives: In our previous study, we have investigated the neural mechanism of the selective listening with the coherence function between a sound envelope to the ear of a subject and the MEG response of the subject. In this study, we compared the EEG response with the MEG response, in order to study the feasibility of EEG-BCI system to support a hearing ability.

Methods: We presented stereo mixture sounds and directed the subject to hear the sound that we appointed beforehand. There were two kinds of mixture sounds, music and voice. We measured two electrical potentials, Cz to the left ear and Cz to the right ear. In both channels, we clearly observed auditory evoked responses, e.g. N100, by using short tone bursts. EEG signals were recorded during sound presentation for 3 min. After preprocessing (off-line filtering and down sampling), values of the coherence function were calculated.

Results: In case of music sounds, the coherence values for the noticed sound were increased like MEG results. However MEG had a clear difference between left and right channels depending on sound lateralization, but EEG didn't have a clear difference between the both channels. Besides, EEG didn't show apparent increase of the coherence values for the noticed sound in voice sounds. We think this is because EEG generally is not so high spatial resolution and the signal are mixed with many components of the brain response. In this measurement, each signal of the left and right channels will be mixed with the responses of both hemispheres. It seems to be a cause to reduce the coherence level.

Conclusion: EEG showed similar results to MEG, yet it needs more spatial resolution to realize EEG-BCI system. The knowledge on the comparison between MEG and EEG might be useful to improve the spatial resolution.

P1-021

MEASUREMENTS OF AUDITORY EVOKED EEG AND MEG BY BONE-CONDUCTED ULTRASOUND IN THE PROFOUNDLY HEARING-IMPAIRED

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Bone-conducted ultrasound (BCU) is perceived even by the profoundly sensorineural hearing-impaired, and a novel hearing-aid using BCU perception, which transmits amplitude-modulated ultrasound by bone-conduction, has been developed. We previously reported that BCU activates the auditory nerve, the brainstem pathway, and the auditory cortex in both normal-hearing and hearing-impaired subjects and hypothesized that the cochlea inner hair cells respond to ultrasound itself with peculiar vibration modes of the basilar membrane. On the other hand, persistent refutation exists that BCU perception depends on generation of audible-frequency components in the transmission path by non-linearity of biological tissue. Various unique characteristics of BCU perception and results of our previous physioacoustical measurements on/around the living human head denied this idea, however, more straightforward neurophysiological evidence is needed. Auditory brainstem responses (ABRs) and auditory evoked fields (AEFs) were measured in the "complete" hearing-impaired who show no measurable hearing sensitivity by the ordinary audiometry.

6 complete hearing-impaired and 10 normal-hearing subjects participated. As BCU stimuli, a 30-kHz tone pip and a 30-kHz tone burst were used in ABR and AEF measurements, respectively. ABRs and AEFs were clearly elicited even in the complete hearing-impaired. In the ABR measurements, waves-I, which indicates compound action potential of the auditory nerve, were clearly elicited even in some complete hearing-impaired subjects. In the AEF measurements, the contralateral stimuli elicited larger and faster responses than the ipsilateral in both complete hearing-impaired and normal-hearing subjects.

The results strongly indicate that BCU perception does not depend on the generation of audible-frequency components. Also, the results push our hypothesis that BCU goes through the normal auditory pathway even though unique processes may exist in the cochlea. Additionally, same effects of stimulation side as air-conducted sound indicate that BCU entered the ipsilateral auditory pathway before branching to the contralateral at the superior olivary nucleus.

P1-022

LEFT AUDITORY SUSTAINED FIELDS REPRESENTING INDIVIDUAL TIME PERCEPTION

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It is known that psychologically perceived time length differs in individuals. We have been investigating the brain areas that represents individual time perception. In this study, time perception parameter α in twelve healthy right-handed adults was determined by a self-answered questionnaire. Subjects with greater α tend to estimate a certain physical time as being longer in general. Besides, auditory and visual sustained fields of the same subjects were recorded by magnetoencephalography.

In the auditory experiment, a chord with durations of 0.8 and 1.6 s was presented binaurally in random order. In the visual experiment, a monochrome drawing by M. C. Escher with durations of 0.8 and 1.6 s was presented in the central visual field in random order. Both auditory and visual stimuli evoked clear sustained fields during the stimulus presentation. The individual dipole moments of the sustained fields were estimated and averaged over 420 – 780 ms (0.8 s in duration) and 420 – 1590 ms (1.6 s in duration)

from the stimulus onset. Dipole moments of the auditory N1m peak were also estimated individually.

In group level analysis, time perception parameter α was positively correlated only with left auditory sustained moments with p=0.026 for 0.8 s in duration and p=0.025 for 1.6 s in duration. That is, subjects with larger sustained dipole moments tended to estimate a certain time as being longer. Significant correlations were not found in the right auditory and visual sustained moments or bilateral N1m moments. The results suggest that the left auditory cortex is related to time perception probably because the area is involved in speech perception in which time perception is essential.

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P1-023

AUDIOVISUAL SPATIAL INTEGRATION DURING LONG-TERM ADAPTATION TO LEFT-RIGHT REVERSED AUDITION

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Long-term exposure for humans to an unusual environment reveals adaptive mechanism of cross-sensory integration. Despite some reports on adaptation to left-right reversed vision achieved with special spectacles, little has been examined about adaptation to reversed audition, partially due to difficulty in reproducing stereophonic space without using large equipments. Here, we successfully developed left-right reversed stereophonic space only using wearable devices, and measured MEG responses under the audiovisual matching task once a week while three participants wore the devices for either four or five weeks. They were asked to discriminate spatially congruent and incongruent (mirror-image) combinations of a tone delivered to either ear and a square cue displayed in either visual hemifield. A feeling of strangeness was gradually reduced from the end of the first week to the final week, and a reversed sound accompanied with visual information was perceived as a unified event from the same (visual) side, unless the direction of the sound was actively discriminated. Similarly, phase-locking of the theta-band MEG signals was gradually increased for congruent stimuli in the superior temporal sulcus from about 200 ms post-stimulus. At the fourth or fifth week, the mean reaction times for incongruent stimuli became shorter than those for congruent stimuli, and this trend resembled a relative increase and decrease in the amplitude of N1m responses for congruent and incongruent stimuli, respectively. These findings suggest that long-term exposure to the reversed stereophonic space caused two types of adaptation: (1) early adaptation occurring in the superior temporal sulcus in which audiovisual errors were compensated based on a newly learned integration rule, and (2) late adaptation occurring in the auditory cortex in which mirror-image audiovisual information was integrated in the plastically modulated auditory system. Consequently, the occipitotemporal network adaptively regulates reorganization of audiovisual information so that humans can adapt to a novel environment.

P1-024

CHANGES IN AUTOMATICITY OF JAPANESE PHONETIC CONTRAST USING THE MISMATCH FIELD COMPONENT

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Numerous studies have consistently demonstrated that first language listeners and most early bilinguals develop automatic selective perception routines (SPRs). The amount of experience with a second language (L2) can result in improvements in L2 phonology, but rarely to a native-like level. We used automaticity of SPRs, measured in the form of mismatch field (MMF) components in a speech discrimination task, as a benchmark for native-like L2 speech perception. To examine the effect of length and intensity of L2 exposure on SPR automaticity, we studied 3 groups of native English speakers: JPII and JPIV groups attended two or four semesters, respectively, of standard-rate college level courses of Japanese (JP). VFT group attended one standard-rate semester and then a very fast track course, which doubles classroom time and covers 30% more material. The study design allowed separation of MMF effects with respect to classroom hours (JPII vs. JPIV) and/or intensity (JPII vs. VFT). To measure automatic L2 brain responses, participants performed a visual attention task while passively listening to auditory stimuli of two JP nonsense words, tado and taado, varying in their vowel duration. Groups JPII and VFT were tested twice, before and after the second semester or fast track course, respectively. Results showed that JPIV had the largest MMF. JPII produced a somewhat weaker MMF at the second relative to the first test, possibly because of habituation in the second scan. The VFT group showed no change across time, possibly because habituation effects were counteracted by enhanced JP perception. These data inform cognitive-perceptual models of L2 learning by revealing how extrinsic measures (amount and intensity of learning) are related to the development of speech perception automaticity. That more intensive learning leads to greater improvements in L2 speech perception than predicted by the overall length of exposure could transform L2 learning approaches.

P1-025

OSCILLATORY CORRELATES OF SENSORY ATTENUATION

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The human brain constantly engages in dynamic predictions about upcoming events. The effect of these predictions on the processing of sensory stimuli can be studied with the sensory attenuation paradigm. Sensory attenuation refers to the phenomenon that self-generated stimuli elicit a weaker sensory evoked brain response compared to externally generated stimuli. However, little is known about the neural mechanism underlying the

effect. We hypothesised that alpha/beta oscillations mediate the sensory attenuation effect by modulating excitability in sensory areas. In this study, we compared the neural responses under the two different conditions for auditory stimuli with MEG in 14 participants. We replicated the reduction of M100 component in the auditory cortex for self-generated stimuli. Following source localisation we performed time-frequency analysis and demonstrated that reduction of M100 is due to a decrease in both power and phase locking in a broad frequency band (3-40Hz). Related to our hypothesis, we found both increased power and phase locking in alpha and beta band in a 400ms window prior to the onset of self-generated stimuli compared to the onset of externally generated stimuli. A decrease in power (beta) and phase locking (theta and beta) for low band oscillations were observed just around the time of stimulus onset. These findings are in line with previous reports suggesting an inhibitory role of alpha/beta oscillations. They also suggest multifaceted mechanisms behind sensory attenuation. Our results indicate that oscillatory activity in sensory areas is controlled by brain mechanisms that predict sensory consequences of actions.

P1-026

AUDITORY NEURAL ACTIVITIES ELICITED BY BINAURAL STIMULI

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In the auditory pathway, contralateral projection is dominant but ipsilateral projection also exists. Therefore, difficultly exists to discriminate neural activities in the auditory cortex responding to concurrent right and left ears' sounds. We have been studying the method that can separate long-latency responses (N1m) in the auditory cortex into the right- and left-ear inputs and the binaural interaction of the two ear inputs using the developed method. We prepared two sets of time series of onset-triggers of stimulus sounds for dichotic stimulus sounds. The two trigger sets had no temporal correlation with each other. Transient evoked responses were much attenuated in amplitude after repeated averaging of the response-epochs using triggers that were asynchronous to the sound onsets, while original waveform of the response was reserved by synchronous averaging time-locked to the sounds. We obtained separated responses to a speech sound /a/ and a 600 Hz pure tone delivered to the right and left ears by using two sets of triggers that were time-locked to the right and left stimuli with random intervals but uncorrelated with each other. Fifteen healthy subjects aged 21 - 26 years underwent MEG recordings with a 122-channel whole-head MEG system. As a result, we confirmed that the contralateral response was significantly greater than the ipsilateral response in dichotic stimulation, though the contra and ipsilateral responses to the speech sound were comparable in the left hemisphere for monaural stimulation. The present method is expected to be applicable to the studies of auditory attention, auditory selection such as cocktail party effect, disorders of auditory processing (APD) and others.

P1-027

NEURAL DYNAMICS OF SENSORY-MOTOR SYNCHRONIZATION

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Our goal was to measure and characterize the interaction between brain regions involved in the perception of timing in music and correlate functional connectivity in the brain with the behavioral results in a sensory-motor synchronization (SMS) task.

We recorded magnetic brain responses while subjects (N=13) performed a tapping task with a rhythmic and metrically structured auditory stimulus. Then, we introduced a sudden change in the metrical structure of the sequence and the subjects had to resynchronize their tapping pattern to fit the new rhythm.

Behavior was assed using 3 measures: Negative Mean Asynchrony, Inter Tap Interval and Time to resynchronize – the time it took each subject to resynchronize with the new pattern following a change in the musical meter.

Source localization was performed using Synthetic Aperture Magnetometry (SAM) beamformer and clusters of significant activation over all subjects were detected using a permutation test between the change in the metrical structure and synchronized tapping. The results indicated a complex network that includes mainly frontal and temporal regions in both hemispheres.

Neuronal connectivity was calculated using Phase Lag Index between couples of significant voxels. Significant correlations were found between the behavioral performance in the tapping task and the functional connectivity in several frequency bands. Moreover, the correlations we found were always such that higher connectivity was positively correlated with better performance in the task.

Our results demonstrate, for the first time to our knowledge, a correlation between neuronal connectivity and performance in a SMS task.

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P1-028

REAL-TIME SINGLE-TRIAL SOURCE LOCALIZATION USING RAP-MUSIC AND REGION OF INTEREST CLUSTERING

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Up to date scanning approaches for the localization of neuronal sources, such as RAP-MUSIC, are hardly able to deliver results in real-time due to their computational effort. RAP-MUSIC source localizations provide not only

feedback about a location of a neuronal active area, but also an insight in correlated processes. This real-time estimation of active functional networks can help to identify cognitive processes with a higher reliability and can therefor help to pivot experimental parameters to subject's reactions during acquisition.

In this work we present a high performance RAP-MUSIC source localization algorithm delivering localizations based on single-trial data in real-time.

We adapted the forward as well as the inverse solution. For the forward solution, we calculate region-wise clusters based on Destrieux's cortical brain atlas, which results in a downsized gain matrix. For the inverse solution, we reduce the computational costs of RAP-MUSIC by modifying and precalculating components of the subspace correlation. Moreover, we apply a modified Powells Conjugate Gradient method, which accelerates the search process. Since the subspace correlations of the RAP-MUSIC are independent, we provide a CPU OpenMP and GPU CUDA implementation to further accelerate the computation.

Our algorithm is able to handle Elekta Neuromag® VectorView™ 306 channel MEG measurements with a sampling rate of 1250 sps. Studies using human MEG evoked data show that the proposed real-time technique is able to handle single-trial raw data using a sliding window approach. We tested the proposed method with data recorded during auditory and somatosensory stimulation. The responses to auditory stimuli are localized in the gyrus temporalis superior on both hemispheres, while somatosensory stimuli lead to activation in the contralateral gyrus postcentralis.

We conclude that our modified RAP-MUSIC algorithm is fast and can localize on single-trial raw data which is a useful addition to common acquisition methods.

P1-029

TIME PRECISION OF CORTICO-CORTICAL INTERACTIONS IN MUSICAL METER FOLLOWING TASK

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We show that the spatial accuracy of the MEG data is better than 4.5 cm and the accuracy for timing of intra cortical coordination is better than 6 ms.

Brain activity was recorded using Magnus 3600 MEG in subjects following changes in musical meter. The subjects heard drum beats at meters of 2/4 and 3/4. The meter flipped between the two possibilities at random intervals. The subjects were asked to follow the beats by tapping with their 2nd and 3rd fingers.

The on-going magnetic fields were converted to current-dipoles over multiple (700 or 565) points over the brain's hull, using Synthetic Aperture Magnetometry. Brief activity undulations were automatically detected in all the current dipoles, at a rate of ~2.5/s. The times of these undulations were treated as point processes. Very clear differences were found when congruent and incongruent taps were compared.

We looked for repeating spatio-temporal patterns of the brief activity undulations. Many (tens of thousands) such repeating patterns were found ranging from repeating triplets of events to repeating patterns of 14 events. The most prominent inter-event-intervals in these patterns were of lags 0 or 1 samples (2 to 4 ms). Specific patterns for each behavior were found.

By teetering the timing of the activity undulations within +/- 1 sample the number of repeating patterns was considerably reduced. This process was repeated while teetering synchronous events in groups of various diameters. With this technique we proved that group diameter can be at most 4.5 cm, and timing accuracy is better than 6 ms.

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P1-030

MEG TEST-RETEST RELIABILITY OF SENSORY OSCILLATIONS

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Stability of neural oscillatory signatures across magnetoencephalography (MEG) measurements is an important prerequisite for basic and clinical research that remains inadequately addressed. Here, we evaluated the test-retest reliability of sensory elicited oscillations in a group of healthy participants (N=10) performing an auditory steady-state-response (ASSR) and a visual-grating task over two MEG sessions.

In the ASSR task participants mentally noted the rare occurrences of pure tones interspersed within a stream of 5Hz or 40Hz amplitude-modulated (AM) tones. In the visual task participants detected a randomly occurring speed-change in the moving concentric grating stimulus. Intra-class correlations (ICC; Shrout & Fleiss, 1979) were derived to assess the strength of spectral power change relative to baseline, the duration of spectral power modulations and/or the inter-trial phase-coherence (ITPC) of task-induced neural oscillations at sensor- and source-level.

ASSR to both 5Hz and 40Hz AM stimuli revealed strong power and phase modulations over bilateral temporal sensors, with longer-sustaining 40Hz relative to 5Hz ASSR. Power modulation strength and duration at 5Hz and 40Hz were associated with lower ICCs compared to ITPC. Source-localization of the 40Hz ASSR with exact low-resolution electromagnetic tomography (eLORETA; Pascual-Marqui et al., 2007) indicated ICCs of ~0.8—0 .9 in bilateral primary auditory regions-of-interest (ROIs).

Visually evoked activity in low-frequency (2—6 Hz) oscillations and induced spectral power decreases in ~8—25Hz frequency range were observed between sessions. Individual peak spectral power modulation in the 40—100Hz range manifested relatively strong reliability (ICC-values of ~0.9),

although corresponding spectral modulation was less reliably sustained. Source localization of the high-frequency (60±20Hz) induced response employing Dynamic Imaging of Coherent Sources (DICS; Gross et al., 2001) yielded ICCs of ~0.7—0.8 in bilateral primary visual ROIs.

Our preliminary sensor- and source-space assessment of auditory- and visually-elicited sensory oscillations shows good test-retest reliability.

P1-031
MEG ANALYSIS OF AUDITORY OBJECT PERCEPTION

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When a musician listens to music (as opposed to a non-musician listener), there is a defined moment in time where he/she recognizes familiar elements (pitch, key, tempo etc...). This temporal process, which can be entitled as 'auditory object perception', is the focus of this research.

We measured brain activity using MEG (Magnus 3600) with an experimental design that focused on higher cognitive processes (scale-identification procedure) as oppose to automatic ones like a percept of sound, dissonance, consonance etc. We applied standard analysis as well as Synthetic aperture magnetometry (SAM) beamformer analysis to obtain estimation of the electrical activity, using the anatomical MRI of each subject. The excellent time resolutions we worked with (scale of milliseconds) allowed us to see fine brain activity dynamics both in time and space. Our results clearly showed differences in brain activity when identification procedure is involved. In particular, it showed steep drop in the alpha and beta ranges at unexpected brain sites following the instance of the defining note.

This work shed light on perception processes and their underlying dynamics.

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P1-032
MODULATION OF AUDITORY EVOKED RESPONSES BY EMOTIONAL IMAGES

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We investigated whether visually presented emotional images modify the auditory steady state response (ASSR) in magnetoencephalogram (MEG). We used the International Affective Picture System (IAPS). Their images allow emotional valence to be systematically investigated. All 200 images were grouped into three categories of "negative", "positive" and "neutral" according to the scores assessed by individual subjects after the MEG measurement. Those images were randomly presented for 2.0 s, in synchronous to a stimulus sound, on a screen in front of the subject. We measured ASSRs elicited by optimized chirp sounds. The stimulus epoch consists of a 2.0 s period of repeated chirps at 20 times/s and a silent period of 1.0 s. The stimulus sounds were delivered to subject's left ear at a sound pressure level 20 dB above sensation. Ten healthy subjects aged 21 - 28 years underwent MEG recordings with a 122-channel whole-head MEG system. A total of more than 50 epochs were recorded for off-line averaging for each condition of negative, positive, or neutral according to the categorization by each subject. The averaged signals were digitally band-pass filtered to 19 - 21 Hz during the 0 - 2.0 s period after the auditory stimulus onset. We then made dipole estimation of the averaged MEG signals and obtained the amplitude of souse waveform in 20Hz component of ASSR recorded over the right temporal area. We found that the amplitude of the ASSR source was larger for the negative than positive impression images (t-test; $p<0.05$). This result suggests that the amplitude of ASSR, which originates from the auditory cortex, was modulated by the emotional images. We speculate that the auditory sensory gating associated with visually-induced negative emotion played a role in the modulation of ASSR.

P1-033
WAVE PACKET ANALYSIS: A NOVEL METHOD FOR TRACKING STIMULUS INDUCED WAVES IN ELECTROPHYSIOLOGICAL DATA

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Intro: A robust means of assessing spatiotemporal characteristics of travelling waves in trial and group averaged induced responses would be beneficial to researchers interested in neural timing and cortical efficiency. We present such a method and provide a proof of principle using a clinical sample of schizophrenia patients and healthy controls.

Methods: MEG data were acquired in 10 patients with schizophrenia and 12 healthy controls during a relevance modulation task. Data were filtered to the theta band and source localised using a beamformer. The envelope of on-going oscillations was computed via the analytic signal. Following this, the amplitude envelope was averaged over trials. In order to perform wave packet analysis (WPA), envelope signals were Fourier transformed and the phase of each Fourier component was incremented by +3.6°. The result was inverse FT'd back and the correlation between the real data, and the phase shifted model computed for all voxels in the head. This was performed iteratively with the phase varied from 0 to 360°.

Results: With increasing phase shift, the spatial location of the peak correlation across all voxels was found to move forward in the head, analogous to a travelling wave. The largest correlations were observed with a phase factor of ~90° in the frontal cortices. We also observed better performance using WPA than with a simple time shift of the data ($p<0.05$). Wave speed was modulated by task condition and patients were found to have less difference between conditions with ANOVA revealing a significant interaction between group and condition ($p<0.05$).

Conclusions: WPA not only provides insight into neuronal brain dynamics, but also provides a robust and simple method for measuring inter-regional wave speed in individuals and groups during performance of a cognitive task.

P1-034
BIMUSICAL BRAINS REVEALED BY MAGNETOENCEPHALOGRAPHY STUDIES

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Like bilingual speakers, bimusical listeners handle two distinct musical-syntactic rules (e.g., tonal schemas) in each musical culture. Neuroimaging studies of bilinguals have accumulated evidence that the pattern of neural activities during syntactic processing of the first (L1) and second (L2) language systems is modulated by several variables such as age of acquisition (AOA) and proficiency level on L2 language; by contrast, little is known about bimusical brains. In this presentation, we summarize our recent magnetoencephalography evidence for listeners' brains shaped by listening experiences of two culture-specific music systems. We find that that Japanese bimusicals' differentiations between tonal processing of the first music system (M1; Western music) and that of the second music system (M2; Japanese traditional music) correlate with dipole location differences in brain regions around the inferior frontal cortex (Matsunaga, Yokosawa, & Abe, 2012). Furthermore, we find that, just as bilingual brains are modulated by the proficiency level of L2 language, spatial distances of dipoles, which are located within brain areas around IFG, for tonal processing of their M1 and M2 systems are shorter in bimusicals who are more proficient in M2 than in those who are less proficient in M2 (Matsunaga, Yokosawa, & Abe, 2014). In addition to the already-published evidence, we argue the influence of AOA of tonal schema of M2 music on the basis of our most recent results of MEG experiment in which brain activity data were obtained from one group of bimusicals exposed to M2 since birth and another group of those exposed to L2 in later development. The discussions of similarties/differences in the influences of AOA and proficiency level on the second systems between bilingual and bimusical brains should contribute to the understanding of our human's unique ability to operate in two culture-dependent communicative sound systems.

P1-035
ASSRS IN MEG TO MUSICAL CHORDS MODULATED IN AMPLITUDE

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Musical chords elicit various emotional feelings while listening to music; for example, major and minor chords cause happy and sad feelings, recpectively. Search for neurophysiological correlates of these behavioral phenomena has attracted many researchers. We measured ASSR (auditory stationary state responses) in MEG to musical chords which were sinusoidally modulated in amplitude. Major and minor chords were used in experiment 1 and 2, and additionally, diminished and augmented chords in experiment 3. In experiment 1 and 3, the modulation frequency was 20 Hz, and in experiment 2, the three constituent tones in each chord were separately modulated by sinusoids of 18.25, 20 and 23 Hz. The ASSRs were larger to the minor chord than to the major chord in experiment 1. In experiment 2, the ASSR to the lowest tone (root tone) of each chord was larger than the other two tones in the chord and also was larger to the minor than to the major chords. Therefore, the difference in power of the ASSR between major and minor chords found in experiment 1 seemed to result from the difference in the responses to the lowest tone. In experiment 3, the power of ASSRs to the 4 categories of chords decreased in the following order: augmented, diminished, minor and major chords. The difference was significant between augmented and major chords. The major chord is the most consonant of the four categories which may well be related to having the smallest ASSR. The augmented chord is different from the other 3 chords in that it cannot be constructed from only the major scale tones but it is not certain whether it is more dissonant than the diminished chord. Curiously, the overall responses were smaller in experiment 3 employing 4 chords than in experiment 1 and 2 with 3 chords.

P1-036
CONNECTIVITY BETWEEN THE HESCHL'S GYRUS AND THE INFERIOR FRONTAL GYRUS MEDIATE THE PROCESSING OF MUSICAL FEATURES IN MOZART VARIATION KV265: A MAGNETOENCEPHALOGRAPHY STUDY

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In our present magnetoencephalography (MEG) study, we examined the connectivity change when listening to real music. In an MEG recording, twenty-one non-musicians (12 females, mean age, 26.5 years; 9 males, mean age, 27.6 years) listened to Mozart Variations KV 265 on the theme of 'twinkle twinkle little star', the familiar song. For first five movements including a theme among the whole musical piece (five conditions), connectivity change between the bilateral Heschl's gyri (HG) and the inferior frontal gyri (IFG) was examined in two target periods, the first and later two second in each movement and in five frequency bands (delta, theta, alpha, beta, and gamma) using Partial Directed Coherence (PDC). The first condition is a theme of 'twinkle twinkle little star', and in the third and fifth conditions is repeated as the same melody. In the second and fifth conditions, a variation of

a theme melody is presented. The rhythm pattern is the same in the second and the third conditions / the fourth and fifth conditions, respectively. In the first target period, the connectivity difference between the five conditions was observed in all bands except the alpha band. The connectivity in beta band differed according to a melody pattern; the connectivity strength in the third and the fifth conditions with the familiar melody were relatively lower than the second and the fourth conditions. In the second target period, the connectivity difference was observed only in gamma band. With our present results, we inferred that the difference of the musical feature could be perceived after two second and found that it was reflected in connectivity between the HG and the IFG. We successfully showed that connectivity measures could be used to explain the change of the musical feature in a real musical piece.

P1-037

IMPAIRED PRE-ATTENTIVE AUDITORY PROCESSING IN FIBROMYALGIA: A MISMATCH NEGATIVITY STUDY

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Fibromyalgia (FM) is characterized by chronic widespread pain and often accompanied by sleep disturbances, fatigue, and cognitive impairment. Patients are more sensitive to sensory stimulation regardless of type and modality, suggesting global problem in sensory processing. The present study for the first time aimed to explore pre-attentive auditory processing, which might be affected as a part of generalized sensory processing dysfunction in FM by measuring mismatch negativity (MMN), a well-suited event-related potential. Also we tried to find a potential association between MMN abnormalities and pain sensitivity in FM. Auditory evoked fields were recorded using magnetoencephalography in 18 right-handed female FM patients and 21 age-, sex- and education-matched right-handed healthy controls (HC) during a duration-deviant auditory oddball paradigm (50-ms standard and 100-ms deviant tones). The magnetic counterpart of MMN (MMNm) was obtained by subtracting the response to standard stimuli from the response to deviant stimuli. Peak latencies, amplitudes and directional asymmetry coefficient (AC) of MMNm amplitude were compared between two groups. Pressure pain threshold over thenar and trapezius muscle was assessed for measuring pain sensitivity. The amplitude of right MMNm was smaller in FM patients than in HC (P=0.020). Directional AC value was lower in FM patients, indicating of more leftward asymmetry than HC (P=0.033). Smaller right MMNm amplitude was associated with lower pressure pain threshold of thenar muscle in FM patients (P=0.003). The present study was the first attempt to investigate pre-attentive auditory processing by utilizing MMNm paradigm between patients with FM and HC, revealing compromised pre-attentive auditory processing in FM as indexed by reduced amplitude, and altered hemispheric asymmetry of MMNm. Also, since MMNm is a marker for cognitive dysfunction, our results would be reflective of cognitive impairments in FM.

P1-038

INVESTIGATION OF THE AUDITORY M100 BRAIN RESPONSE FOR LOW FREQUENCY SOUND STIMULATION

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Auditory evoked magnetoencephalographic (MEG) responses are well documented for stimulation with pure tones between 500 Hz and 8 kHz. Especially the m100 response is of particular interest. It is a sign of hearing and it encodes parameters of the stimulus by changing latency, amplitude and morphology. We investigated the variation of the m100 response towards low frequencies covering the range from 250 Hz down to infrasound of 12 Hz. Understanding hearing processes at very low frequencies is important for regulatory purposes and noise assessment.

To perform the study an MEG compatible infrasound source was designed and manufactured. Subjects' individual loudness perception was tested before the measurements to provide constant subjective loudness across the frequency range. A 128 channel gradiometer MEG-system (Yokogawa) in a magnetically shielded room was used. The stimuli were pure sine tones at frequencies of 250 Hz, 125 Hz, 63 Hz, 40 Hz, 20 Hz and 12 Hz. The frequency was measured with an optical microphone during measurement. All subjects reported a perception down to 12 Hz.

Frequencies were presented in random order and each tone was presented 80 times. From the averaged responses the latency and amplitude of the m100 were estimated. The underlying generators were reconstructed using a simple two dipole fit in a homogeneous conductive sphere.

Responses to stimuli above 63 Hz showed a typical m100 pattern. Their generators were located in the region of the auditory cortex. Below 63 Hz, the dipole pattern gets masked by spontaneous brain activity and their generators slightly move towards central. M100 amplitude decreased with decreasing frequency although the tones were presented at constant subjective loudness. The latency of the m100 response remained stable at 120 ms for all frequencies. This behavior is not known for the m100 response for auditory stimuli between 500 Hz and 8 kHz.

P1-039

AUDITORY ENVELOPE FOLLOWING RESPONSES IN THE MATURE AND DEVELOPING BRAIN

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Recent theories of speech perception propose that speech envelope plays a crucial role in speech perception by aligning brain excitability patterns with the intensity fluctuations of the speech sounds. The present two

experiments tested two main hypotheses derived from these theories: (1) That the speech envelope provides crucial cues for temporal encoding of acoustic sounds; (2) that temporal encoding is not fully mature in preschool-aged children (3 to 5 years old). Using an amplitude-modulated broadband noise swept from 1 to 80 Hz, an envelope following response was demonstrated continuously tracking the modulation rates in mature adult brain but not in preschool-aged children. Temporal modulation transfer function reflecting the phase-locked transient responses in following the temporal modulations identified preferential frequencies for phase-locking and hemispheric differences in these preferential frequencies, which were significantly different between mature and immature brain. We concluded that the human auditory system has high sensitivity to encode temporal modulations embedded in sound envelope, but this high temporal sensitivity is not fully acquired in young children.

P1-040

MELODIES IN THE BRAIN

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Musical melody recognition may serve as a typical example of a dynamic perceptual process. A melody is generally composed of tones and rhythm. The process of melody recognition is presumably gradual, with each tone providing additional cues to the listener, until final recognition of the melody is achieved. The current study examined brain processes involved in the recognition of famous melodies. We used the high temporal and spatial resolution of the MEG signal to reliably examine the evolving brain signal throughout the different phases of melody recognition. Twenty five participants heard famous melodies, and had to indicate whether they were familiar with them. An additional behavioral test, performed after the MEG session, examined the participants' acquaintance with the song names. The MEG signal was analyzed, searching for dynamic developments during the time course of the melody. A significant, nonlinear reduction in signal intensity was detected, indicating a possible top-down influence of recognition on brain activity. Phase lag index analysis also gave additional information, demonstrating a bell shaped connectivity curve in the time course of listening to a melody. Taken together, these results support the conjecture of a gradual melody recognition process, culminating in full recognition, which is followed by a decrease in both intensity and connectivity in overall brain activity.

P1-041

HUMAN CORTICAL RESPONSES TO SLOW AND FAST BINAURAL BEATS REVEAL MULTIPLE MECHANISMS OF BINAURAL HEARING

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When two tones with slightly different frequencies are presented to both ears they interact in the central auditory system and induce the sensation of a beating sound. At low difference frequencies, we perceive a single sound moving across the head between the left and right ears. The percept changes to loudness fluctuations, roughness, and pitch with increasing beat rate. To examine the neural representations underlying these different perceptions, we recorded neuromagnetic cortical responses while participants listened to binaural beats at continuously varying rate between 3 Hz and 60 Hz. Binaural beat responses were analyzed as neuromagnetic oscillations following the trajectory of the stimulus rate. Responses were largest in the 40-Hz gamma range and at low frequencies. Binaural beat responses at 3 Hz showed opposite polarity in the left and right auditory cortices. We suggest that this difference in polarity reflects the opponent neural population code for representing sound-location. Binaural beats at any rate induced gamma oscillations. However, the responses were largest at 40-Hz stimulation. We propose that the neuromagnetic gamma oscillations reflect post synaptic modulation that allows for precise timing of cortical neural firing. Systematic phase differences between bilateral responses suggest that separate sound images exists in the left and right auditory cortices. We conclude that binaural processing at the cortical level occurs with same temporal acuity as monaural processing whereas the identification of sound location requires further interpretation and is limited by the rate of object representations.

P1-042

ALPHA SUPPRESSION IN CI PATIENTS WITH SSD REFLECT POST-IMPLANTATION INCREASE IN HEALTHY EAR COMPREHENSION OF DEGRADED SPEECH

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Objectives: The effects of cochlear implantation on healthy ear comprehension of degraded speech in patients with single-sided deafness (SSD) are examined using behavioral and electrophysiological measures.

Background: The suppression of auditory alpha oscillations during speech processing has been shown to be correlated with the level of comprehension of spectrally and temporally degraded words. Since cochlear implants (CIs) present the wearer with spectrally degraded speech while leaving the

temporal envelope intact, it is expected that processing of spectral and temporal speech degradation will be affected by CI implantation.

Methods: In a cohort of 4 adult CI patients with late-onset SSD, words were presented to the healthy ear with varying degrees of spectral and temporal degradation via vocoding and envelope smoothing. This was done in two sessions – preoperatively and 3 months post-implantation. Neural responses were recorded using 128 channel EEG. Additionally, patients were asked to rate their level of comprehension for each word.

Results: Behavioral measures and greater alpha-suppression over a cluster of parietocentral electrodes reflect an increase in comprehension post-implantation for temporally degraded speech, but not spectrally degraded speech.

Conclusions: These initial improvements in comprehension of temporally degraded speech may represent an increased reliance on temporal envelope cues by the implanted ear. A resulting healthy ear benefit could indicate shared speech processing pathways with the implanted ear. Further work will determine if there is a correlation between implanted ear and healthy ear processing of degraded speech.

P1-043
CORTICAL DYNAMICS ELICITED BY ILLUSORY AND NON-ILLUSORY AUDITORY STIMULI

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Aims: When a dichotic pair of tones spaced an octave apart is repeatedly presented in alternation, the Deutsch's octave illusion may occur, so that a single tone that alternates in pitch between ears is perceived (Deutsch 1974, Nature). We here present a MEG experiment to study which are the involved regions and which is their temporal sequence of activity during the Deutsch's illusion. Specifically, we compared here the neural correlates of three acoustic stimulations: the illusory sequence itself, a monaural stimulation mimicking the percept, and a sequence similar to the illusory one in which the tones are far closer in frequency, and which does not elicit the illusion.

Methods: The sequence of the experimental condition is composed of the 400 and 800 Hz tones constituting the dichotic pairs (400 Hz left, 800 Hz right; 800 Hz left, 400 Hz right), lasting 500 ms. For control purposes, the monaural stimulation composed by 800 Hz in the left ear followed by 400 Hz in the right ear, and so on was presented. Finally, a non-illusory sequence similar to the illusory sequence, in which the frequency of the two tones was 400 and 480 Hz, was presented. MEG signals were recorded by a 165 channel whole-head system. Whole head activity was studied through Loreta.

Results: Significant activities were found in the bilateral Heschl gyrus, the insular cortex, in the IFG and MFG, and in the left IPL. Preliminary results showed higher amplitudes following the illusory sequence in all these regions up to the middle (20-250 ms) latencies. Although only small amplitude differences were found in the latest latencies (250-400 ms), peak responses were slower in the ILL condition. The circuit we found extends to illusory perception the what-where processing mechanisms observed in auditory cortical areas.

P1-044
ABNORMAL BRAIN SYNCHRONY IN CHILDREN WITH DOWN SYNDROME

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The auditory steady state response (ASSR) is an oscillatory brain response to auditory stimuli that shows maximal amplitude when the stimulus or modulation rate is near 40Hz, and has been used in the study of developmental disorders such as Down Syndrome (DS). Recent evidence shows that the ASSR in children with DS shows greater phase spread relative to normal children, suggesting potential differences in neuronal synchronization within the brain. We thus hypothesized that these synchronization issues will also manifest as lowered power in the steady state frequencies as well as more distributed activity in topographical scalp projections.

We used magnetoencephalography (MEG) to study the ASSR in 6 participants with DS (aged 9-12) and 9 age-matched healthy controls. Stimuli consisted of 10s tones with 500ms interstimulus interval, with amplitude modulation at 40Hz. Data were collected at the Down Syndrome Research Foundation in Burnaby, British Columbia. Preliminary results using wavelet and independent component analysis suggest lower ASSR power in some DS participants compared to healthy controls. In addition, this power reduction is confirmed with polar plots, which also demonstrate greater phase dispersion in DS relative to control. There appears to be a more diffuse activation pattern in topographical scalp projections in DS compared to healthy controls. These preliminary results suggest that the ASSR in DS children exhibit less phase coherence relative to control, and the diffuse pattern of activation in DS is also consistent with greater neuronal de-synchronization, which in turn leads to a reduction in overall ASSR power. These changes may reduce the efficiency of neuronal firings in DS, which increases the difficulty of cognitive tasks such as attention and resource allocation. This may in turn contribute to the cognitive and attentional deficits seen in children with DS.

P1-045
INVESTIGATION OF AUDITORY OFF-RESPONSE TO PURE TONE STIMULATION BY USING MEG

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A 128 channels helmet-shaped first order low-*Tc* axial gradiometer SQUID magnetoencephalography system was used to study the auditory evoked off-response which emerges about 100 ms after the cessation of sound. The sensitivity of axial gradiometers showed an averaged noise level of 3.5 fT/

Hz1/2 at 100 Hz inside a magnetically shielded room. The measurements were performed with the monaural 250 Hz pure tone stimuli of 80 dB sound pressure level persisting for 425 ms to the left or right ear of subjects. The auditory evoked field around 100 ms after the stimuli onset is defined as N100m, and that around 100 ms after the cessation of stimuli is defined as off-N100m. The software CURRY was used to calculate the source locations of equivalent current dipole of N100m and off-N100m. The spatial distribution of the equivalent current dipole of N100m and off-N100m were investigated and analyzed. It was found that the locations of equivalent current dipole of off-N100m were more interior than that of N100m, which implied different neuron activities in the auditory cortex. We also found that the appearance probability and the peak latency for the off-N100m extraordinarily exhibit right-dominant hemispheric asymmetry. Based on these observations we speculated that off-N100m is an independent event which could induce the neuron activity different from N100m in the human auditory cortex. The experimental data suggested that human brain uses different neurons in the auditory cortex to process the information about the onset and cessation of a sound.

P1-046
HOW TO ADAPT MAGNETORELAXOMETRY ACTIVATION SETUPS FOR QUANTITATIVE MAGNETIC NANOPARTICLE IMAGING UNDER REALISTIC NOISE CONDITIONS

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Magnetic nanoparticles (MNP) are increasingly applied in biomedical applications due to their high saturation magnetization, which makes them detectable at a distance, and their small diameter, which allows them to reach virtually every region in the body. These applications require an accurate knowledge of the spatial MNP distribution to operate efficiently. Magnetic nanoparticle imaging based on magnetorelaxometry (MRX) is a promising technique to recover the MNP distributions quantitatively. An array of magnetic sensors (i.e. SQUIDs) measures the relaxation of the net magnetic moment of MNP distributed in a volume after a magnetizing field is switched off. The activation setup encompasses an array of coils generating the magnetizing field.

In this study, we want to maximize spatial sensitivity throughout the volume while simultaneously reducing the number of coils so to speed up the measurement. Therefore, two MRX activation setups for the imaging of rat- and rabbit-sized objects are numerically optimized for accurate MNP reconstructions. Our simulations employ realistic noise models which allow a more accurate determination of MRX performance compared to the Gaussian white noise model (difference in simulation and experimental results of ≈ 0.2% and ≈ 2.5 % respectively). We analyze how the activation setup needs to be adapted when prior information on MRX noise is available, and when the required sample volume and (possibly non-uniform) resolution is known. Furthermore, we study improvements in reconstruction quality when using non-uniform reconstruction grids based on MRX noise. The noise information for the calculations originates from noise measurements performed with a 304 SQUID vector magnetometer system.

The adaptation considers the number of coils, their diameters, currents and orientations and their distances with respect to the sample. Considering realistic noise reduces the number of coils from 48 to 18, thereby reducing measurement time while obtaining a 4 times larger sensitivity towards smaller MNP concentrations.

P1-047
MAGNETIC PARTICLE SPECTROSCOPY TO QUANTIFY THE MAGNETIC NANOPARTICLE DISTRIBUTION IN BIOLOGICAL TISSUE

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Magnetic nanoparticles (MNP) open new pathways in cancer therapy and non-invasive diagnostics. For development of magnetic hyperthermia and magnetic drug targeting applications it is of vital importance to have sophisticated techniques to quantify the MNP distribution within a body. Magnetic particle spectroscopy (MPS) specifically detects the nonlinear magnetic response of MNP exposed to an oscillating magnetic field. The amplitude of the MPS signal is proportional to the MNP amount in the sample. Biological tissue and paramagnetic blood iron do not contribute to the MPS signal.

We demonstrate the ability of this quantitative magnetic technique for sensitive and specific (unaffected by body iron) MNP detection in blood and tissue samples after intravenous application of MNP (two different MNP types at 0.3 mmol/kg body weight and 1 mmol/kg body weight dosages) in a mice model. To this end we determined from blood samples taken before and at t=2, 5,15, 30, 45 min after injection MNP half-lives and their organ uptake after 45 minutes of circulation. We found dosage and MNP dependent half-lives between 20 min and 100 min. Accordingly, most of the MNP were already accumulated in the liver after 45 min circulation.

MPS allows fast and reliable detection of SPIOs in tissue samples. Due to its high sensitivity only small sample volumes of 10 to 100 nanograms of SPIO iron per sample are required for a safe SPIO quantification not hampered by natural body iron.

P1-048
DIPOLAR INTERACTIONS BETWEEN MAGNETIC NANOPARTICLES IN MAGNETORELAXOMETRY

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In recent years, many biomedical applications based on magnetic nanoparticles such as disease detection, targeted drug delivery and hyperthermia have emerged. All of these applications rely on an accurate knowledge of

the spatial distribution of the magnetic particles and thus require a nanoparticle imaging technique. A promising imaging technique is magnetorelaxometry (MRX). However, despite a thorough theoretical knowledge of the magnetization dynamics of a single particle, the estimation of the spatial distribution of the particles still might be inaccurate due to the collective behavior of the nanoparticles which is not taken into account in the theoretical model supporting MRX

Numerically investigating these particles from first principles (i.e. micromagnetically) will lead to an understanding of this collective behavior and consequently to an improved performance of aforementioned applications. To this end, we verify theoretical assumptions supporting the interpretation of MRX data with the simulation software Vinamax. This in-house developed package enables full micromagnetic simulations of ensembles of nanoparticles and takes into account dipolar, thermal, anisotropy and externally applied fields.

When interpreting MRX data, an important theoretical assumption is that the magnetic particles are located sufficiently far apart to neglect the dipole-dipole interaction between different particles. By determining the relaxation constant as function of nanoparticle concentration, we verify if this assumption is justified for concentrations typically used in experiments (up to 60 µg iron per g tissue). We also provide an estimate for the concentration for which this assumption does not longer hold, and how the dipole-dipole interaction influences the magnetic relaxation.

Furthermore, with Vinamax it is possible to investigate other aspects of MRX such as the initial magnetization procedure or the consequences of an inaccurate knowledge of the particle size distribution on the nanoparticle distribution reconstruction.

P1-049

DEVELOPMENT OF A RABBIT SIZED PHANTOM FOR VALIDATION OF QUANTITATIVE IMAGING OF MAGNETIC NANOPARTICLE DISTRIBUTIONS

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For novel biomedical applications of magnetic nanoparticles (MNP) like magnetic drug targeting or magnetic hyperthermia the quantitative knowledge of the MNP distribution inside a body is essential. Several MNP specific imaging modalities (e.g. Magnetic Particle Imaging (MPI) and magnetorelaxometry (MRX)) are potentially able to accomplish this task. A necessary prerequisite for the validation of these imaging modalities in terms of quantitative reproducibility and feasibility under pre-clinical conditions is a suitable phantom with well known properties. We developed a rabbit sized phantom that was designed according to the experience gained in a previous in-vivo MNP imaging study where the therapeutic efficiency of magnetic drug targeting was investigated in rabbit tumor models by MRX. The diamagnetic phantom body made of Plexiglas® (l = 50 cm, b = 40 cm, h = 8 cm) reflects a typical rabbit. Gypsum cubes (1cm3) homogeneously loaded with MNP serve as basic component to model complex MNP distributions. Two supports inside the phantom (capable to house 320 (8Nx 8Ny 5Nz) MNP loaded cubes) offer the possibility to generate MNP distributions at spatially distinct body regions (tumor region at hind leg and liver-lung region) of a rabbit. Additionally, vessels can be used as well to model MNP injection during drug targeting therapy. Defined drills located at the top and bottom of the phantom guarantee an accurate positioning of marker and/or excitation coils with a fixed position relative to the MNP distribution that shall be investigated in the magnetic measurements. The phantom was used to investigate the quantitative reconstruction of an MNP distribution by spatially resolved MRX. Our results demonstrate that the phantom is a suitable tool for providing complex and reproducible MNP distributions with defined conditions in terms of geometry and MNP content for validation of MNP imaging techniques preparing the application in pre-clinical environments.

P1-050

NUMERICAL ANALYSIS OF THE INFLUENCE OF MAGNETIC PROPERTIES ON THE THERMAL DISTRIBUTION DURING MAGNETIC NANOPARTICLE HYPERTHERMIA

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Magnetic nanoparticle hyperthermia is an auspicious alternative cancer treatment that creates heat by means of magnetic nanoparticles. This work numerically investigates the temperature and damage in biological tissues due to the presence of a distribution of magnetic nanoparticles.

The heating power of magnetic nanoparticles in the presence of an alternating magnetic field is calculated by means of the linear response theory (LRT). LRT is a model that describes the dissipation mechanisms based on the rotational relaxation (both Néel and Brownian relaxation) of single domain magnetic nanoparticles. The main assumption of this model is that the magnetic system responds linearly with the applied magnetic field. Therefore, the LRT results in a power density that is proportional to the imaginary part of the susceptibility, the frequency and the square of the amplitude of the oscillating magnetic field. This magnetic heat source is then added to the Pennes' bioheat model which includes the traditional heat conduction and the effect of blood perfusion.

To gain insight in the macroscopic effect of magnetic nanoparticle hyperthermia, we implemented a 3D-FD model, based on LRT and the Pennes' model, on a regular cubic grid with a spacing of 1mm. The spatial distribution of the nanoparticles is considered to be Gaussian. The 3D-FD model is able to calculate the temperature in the tumor and surrounding healthy tissue by using the modified midpoint method and an additional Gragg-smoothing. Starting from the temperature, we determine the survival rate by means of an Arrhenius model. The survival rate can be interpreted as the concentration of living cells at a certain time compared to its initial concentration. We modulate the blood perfusion term of the Pennes' model with this survival rate. Additionally, the 3D-FD model allows us to assess the influence of the field amplitude, frequency and the concentration of the particles.

P1-051
MAGNETIC CHARACTERIZATION OF NANOPARTICLES FOR SUSCEPTIBILITY BASED IMAGING

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The objective of the present study is characterize the nonlinear, frequency-dependent, complex magnetic susceptibility properties of mNPs in support of alternating current (AC) susceptibility imaging research. The use of iron oxide magnetic nanoparticles (mNPs) in targeted cancer hyperthermia is an active area of research with great promise for improving cancer treatment efficacy. Cancer-cell-targeted mNP hyperthermia, alone or in combination with conventional therapy, can provide a higher therapeutic ratio, and has the potential to treat small, undetected metastases. Although several hyperthermia-based cancer therapies are currently approved for use, their effectiveness and clinical translation have been limited by the lack of technology for real-time image guidance. Imaging is needed to quantify the mNP distribution in the tumor and surrounding tissue prior to commencing particle heating with an alternating magnetic field. However, clinical imaging modalities like computed tomography (CT) and magnetic resonance imaging (MRI) are not efficacious in imaging mNPs at the high concentrations that are required for cancer hyperthermia applications so experimental methods of imaging mNPs are being investigated. Our previous research demonstrated a method for magnetic susceptibility imaging that combines multi-frequency AC magnetic susceptibility measurement with a tomographic imaging array of drive coils, compensation coils and fluxgate magnetometers. This system allows for susceptibility magnitude imaging and spectroscopic AC susceptibility imaging. Previous results also proved the concept of spectroscopic susceptibility imaging using low-cost instrumentation that is adaptable to the intraoperative setting. Quantitative imaging of mNPs with this system requires detailed knowledge of the magnetic behavior of these iron oxide mNPs. Specifically this requires measurement of the nonlinear, frequency-dependent, complex magnetic susceptibility mNP responses and determination of whether these behaviors fit existing models of mNP magnetic characteristics. This data will allow for quantitative mNP imaging as well as calibration and optimization of the AC susceptibility imaging system.

P1-052
DEVELOPMENT OF HIGH SENSITIVE AC BIOSUSCEPTOMETER FOR MAGNETIC NANOPARTICLE IMAGING

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A High Sensitive Alternating Current Biosusceptometer (HS-ACB) and a computerized 3D table to acquire magnetic images are presented. The ACB consists of two pairs of coils separated by a fixed distance (baseline) in a first-order gradiometric configuration, where each pair is composed of an excitation coil and a detection coil. The pair (excitation/detection), located more distant from the magnetic sample acts as reference. The ACB employed in this work consists of two identical pickup coils connected in gradiometric arrangement (500 turns, ø = 10 mm, and h = 10 mm), and two pickup coils connected directly in series (150 turns, ø = 14 mm, and h = 10 mm) producing an alternating magnetic field (2 mT rms, 10 kHz). The baseline was 150 mm. An electronic circuit was developed in association with a lock-in amplifier to improve ACB sensitive. A software routine was developed to control the position and time of scanning. The data were collected by changing the position of the sensor on the array of 80 x 80 mm in steps of 5 mm. A map of 17 x 17 points was acquired and the image was created and post-processed. The sensitive was characterized by a magnetic pill (ø = 10 mm, and h = 5 mm) with 0.5 g of ferrite homogenized with excipients. The HS-ACB was used to acquire images from micro-drops of magnetic nanoparticle. The ACB output signal was improved from 2.3 V to 9.1 V, a gain of 12 dB, and the sensitivity dependence with distance was improved from 62.0 mm to 87.0 mm. The HS-ACB obtained images of nanoparticle drop of 2 µL (50 µg of ferrite), a value 60% lower than previous ACB designs, resulting into good prospects for investigations of the magnetic nanoparticle distribution.

P1-053
TWO-DIMENSIONAL NMR SPECTROSCOPY OF 13C METHANOL AT 5 µT

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Nuclear magnetic resonance at Ultra-Low Field regime (ULF-NMR) has paved the way for novel biomedical measurements, such as chemical analysis of molecules based on J–coupling spectrum,[1] functional connectivity imaging using brain wave source,[2] etc.

The ULF-NMR requires the special technique of circularly polarized pulses for pulsed NMR experiments, because conventional pulses, which are linearly polarized, can not drive nuclear spins coherently owing to the Bloch-Siegert (BS) effect. We experimentally verified that this issue can be resolved by applying circularly polarized fields using two orthogonal coils.[3] The nuclear spins can be driven coherently with the circularly polarized pulses. This method makes it feasible to employ multiple pulse sequences in ULF-NMR studies.

Using circularly polarized pulses, for the first time, we conducted two-dimensional NMR experiment of methanol, 13C enriched up to 98 %, at 5 µT. Since the J(CH3) coupling (~ 140 Hz) is comparable to the 1H resonance frequency (~ 200 Hz), the COSY spectrum produces the most complex pattern, which in turn can be exploited as a fingerprint of the CH3 ligand.[4] The 2D spectrum is certainly more confirmative for chemical analysis than 1D spectrum. In addition, we demonstrate that compressive sensing can effectively reduce the time cost required for the 2D measurement.

We believe further application beyond the two dimensional spectroscopy will be accessible by using circularly polarized pulses in ULF-NMR, i.e., structural determination of molecules using 3D NMR spectrum.

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P1-054

ABNORMAL NEURAL ACTIVATIONS DURING A MENTAL FLEXIBILITY TASK IN SOLDIERS WITH POST-TRAUMATIC STRESS DISORDERS (PTSD)

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Background: PTSD stems from exposure to one or more events that involve actual or threatened death or serious injury. While PTSD is thought to involve a dysregulation of emotional neurocircuitry, individuals with PTSD also report neurocognitive difficulties. Mental flexibility is a core executive function that reflects the ability to adapt and shift within new environments. It is essential for appropriate social-cognitive behaviours. MEG has been used to track the progression of brain activation during set-shifting, a measure of mental flexibility. We hypothesized that MEG would capture the interaction between the abnormal neurocircuitry implicated in PTSD and brain regions involved in set-shifting.

Methods: 22 soldiers with PTSD and 24 matched control soldiers completed a colour-shape set-shifting task. MEG data were recorded continuously and beamforming was used to source localize brain regions involved in the task; the beamformer images were submitted to an image contrast between groups. Virtual sensors were reconstructed from regions showing significant activation on source localization and submitted to statistical testing to identify latencies when activations in a specific area were significantly different between groups.

Results: The control group showed a sequence of activity that involved dorsolateral frontal cortex, insula and posterior parietal cortices, as expected from the literature. The soldiers with PTSD showed these activations but they were interrupted by activations in paralimbic regions, namely posterior cingulate and parahippocampal gyrus.

Conclusions: These findings are consistent with models which suggest that PTSD results from dysfunctional neurocircuitry. Specifically, it is thought that the limbic areas are hyper-reactive. In tandem, frontal areas are under-active and thus fail to appropriately modulate the limbic activity. This is the first demonstration that MEG can identify the timing and location of atypical neural responses in PTSD with a set-shifting task. These data support the model that hyperactive limbic structures can negatively impact cognitive function.

P1-055

OPTIMIZING FMRI AND MEG FOR PRESURGICAL MAPPING

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Background: Functional MRI (fMRI) and magnetoencephalography (MEG) are tools for pre-surgical mapping. For clinical application, both must demonstrate spatial specificity, and robust/reliable activation patterns. We have developed a protocol for optimization of pre-surgical mapping using a receiver-operator curve framework (ROC-r), and applied it to both fMRI and MEG. We present a comparison of our results in a group of healthy volunteers, and in patients with intracranial tumours. In the patient cases, intraoperative electrophysiological measures were recorded to validate the pre-surgical mapping.

Methods: 10 healthy volunteers had both fMRI and MEG scans. Participants performed a combined language/motor task 3 times within each session. Participants decided if 90 visually-presented pairs of English words were semantically related (50%) or unrelated (50%), and responded with the left/right hand respectively. Patient volunteers performed the same task prior to surgery.

The fMRI data were motion corrected, high-pass filtered, spatially smoothed, and pre-whitened. Two GLM models were used: 1) left vs. right hand and 2) matched and unmatched word reading.

MEG data were band-pass filtered, and epochs were extracted relative to 1) left/right forearm EMG onset, and 2) the first word of the word pairs. An MRI-based head model combined with the dynamic statistical parametric mapping approach was used to produce volumetric t-statistic maps at selected latencies.

ROC-r was used to optimize data processing options and assess inter-scan reliability. These optimized maps were compared to the intraoperative electrophysiological measures.

Results/Conclusion: Optimized motor maps for both fMRI and MEG reliably included the pre-/post- central gyri around the hand knob. For language mapping, fMRI reliably produced lateralized inferior frontal lobe activation, and occasional superior temporal lobe activity. MEG produced robust lateralized activation of the posterior-superior temporal lobe, with more variable results in the frontal lobe. We also show illustrative patient cases in which intraoperative recordings validate the pre-surgical maps.

P1-056

LONG-TERM CYCLIC MENSTRUAL PAIN CHANGES EMOTIONAL PROSODY PROCESSING IN PRIMARY DYSMENORRHEA FEMALES

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Primary dysmenorrhea (PDM) is the most common gynecological disorder for reproductive females. Functional MRI studies showed altered brain structures and functioning in PDM females (PDMs). Although literature pointed out possible links between pain and emotion, the effect of long-term cyclic menstrual pain on emotional processing is yet unveiled.

60 PDMs and 69 age-matched female controls both with regular menstrual cycle were recruited. Whole-head 306-channel MEG (Elekta, Neuromag) was used to investigate brain responses to emotional prosody processing of neutral, happy, sad and angry voices during menses (Day 1-3, MENS) and peri-ovulatory (Day 12-14, POV) phases. Psychological inventories and pain experience were also collected. Peak amplitude and peak latency of M50 and M100 auditory evoked fields and their peak-to-peak (P2P) amplitude and latency were identified in each individual, and correlations were studied.

Overall, PDMs reported significantly poorer personal emotional adjustment and lower quality of life, also significantly higher levels of anxiety and pain catastrophizing than controls in both menstrual phases. PDMs showed shorter M100 peak latency to neutral and sad voices than controls during POV, and shorter latency to neutral and happy voices during MENS. Correlations were found between pain catastrophizing and P2P latency of happy voice in controls but not in PDMs during POV; during MENS, the higher scores on negative personality scales, the longer the peak latencies were found in PDMs but not in controls.

On the other hand, while controls did not report any psychological differences between phases, they responded to emotional prosody voices mainly with shorter peak latency and/or larger peak amplitude during MENS. On contrary, PDMs reported significantly higher levels of anxiety and pain catastrophizing during MENS, but no AEF differences between phases. Results might imply that after long-term cyclic menstrual pain, PDMs' brains are "trait-shaped" so vastly that their brain functioning are similar between phases.

P1-057

INCREASED ALPHA-BAND PHASE SYNCHRONISATION IN PTSD DURING WORKING MEMORY AND DELAYED RECOGNITION

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Post-traumatic stress disorder (PTSD) is a serious mental health injury characterised by hyperarousal, re-experiencing, emotional numbing and avoidance. The disorder can manifest after experiencing a traumatic life event, and its prevalence in combat-deployed military personnel is higher than the general population. Whilst its aetiology and resultant symptomology are fairly well understood, little is known about potential changes in neurophysiology underlying secondary psychological sequelae observed in the disorder. In particular, it is unknown whether changes in functional connectivity mediated by neural synchronisation may be linked to cognitive deficits. Here, using MEG, we identified atypical alpha-band phase synchronisation in a combat-related PTSD population during a working memory (1-back) and delayed recognition task that included emotionally-salient and neutral pictures. We show that the PTSD group performed with decreased accuracy in the 1-back working memory task for neutral stimuli, and this was accompanied by long-range hypersynchronisation in the alpha-band during encoding-maintenance and recognition, when compared to matched combat-exposed controls. Increased synchronisation was mainly confined to sources in temporal and frontal regions, predominantly in the left hemisphere, during both aspects of the task. This pattern was maintained in a subsequent paradigm probing delayed recognition of the emotionally-salient images (intermixed with neutral and foil images). Here, using 2-alternative forced choice, participants responded to whether images were novel or repeated. Elevated alpha-band phase synchronization was observed in the PTSD group in a distributed network of brain regions, particularly the amygdalae and fusiform, regions implicated in the processing of emotionally-relevant stimuli. Consistent with literature that suggests large-scale alpha synchrony facilitates working memory-processing, these results suggest that enhanced and atypical neural synchronisation may contribute to the working memory deficits seen in PTSD, and that hyperconnectivity in emotional and memory-related regions may be a factor in one of the principal symptom clusters of PTSD, the re-experiencing of traumatic events.

P1-058

LANGUAGE LATERALIZATION IN PRE-SURGICAL MAPPING USING VOLUME-BASED MNE APPLIED TO MEG DATA

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The use of functional neuroimaging holds the promise of improving neurosurgical outcomes by providing preoperative localization of critical brain

functions. Of particular interest to many neurosurgeons is that of language lateralization. While the brain representation of language function has been localized using magnetoencephalography (MEG) in neurotypical participants, the best corroborative laterality evidence comes from comparison with the invasive techniques that often accompany neurosurgical planning, such as the gold standard Wada test. The present report compares the language lateralization results of MEG and Wada tests for 12 epilepsy patients who underwent resection or depth electrode placement in language-critical regions, and reports these patients' surgical outcomes. All patients completed three language tasks while in the MEG: Dichotic Word Listening, Object Naming, and Word Reading. After standard pre-processing, source localization was completed by volume-based MNE calculations utilizing a realistic boundary element model. MEG language lateralization was determined by the convergence of lateralization across the three language tasks. For all but two patients, lateralization results from MEG and Wada matched. The two patients who did not match were indicated as left lateralized in MEG but bilateral in Wada and neither patient suffered persistent speech impairment post-surgery. Three patients experienced some transient speech impairment post-surgery but recovered. One patient, who was found to be left lateralized by both MEG and Wada, had persistent speech impairment after a surgery that necessarily resected both left frontal and left temporal regions. Overall, the high degree of concordance between MEG and Wada results (83% agreement) is consistent with previous findings (Papanicolaou et al, 2004) but additionally confirms the efficacy of using a distributed source method such as volume-based MNE in pre-surgical mapping cases. Combined with the low rate of post-surgery deficit, these results continue to assert the valuable role of MEG as a non-invasive pre-surgical mapping tool.

P1-059

HIGH FREQUENCY OSCILLATORY STATE IN SOMATOSENSORY EVOKED MAGNETIC RESPONSES MAY PREDICT RESIDUAL BRAIN FUNCTION IN PATIENTS WITH MINIMALLY CONSCIOUS STATE

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Patients with head trauma after traffic accidents often suffer from diffuse axonal injury (DAI). In this study, we aimed to evaluate residual brain function of patients with minimally conscious state (MCS) with magnetoencephalography (MEG). Twenty-eight MCS patients (ages, from 18 to 81; 20 males) and 51 healthy volunteers (ages, from 20 to 75; 25 males) were included in this study. Written informed consent was obtained from subjects or persons who have parental authority of the MCS subjects, according to the guidelines of the local ethical committee and the Declaration of Helsinki. We evaluated somatosensory evoked magnetic responses (SERs) for median nerve stimulation with a whole-head MEG system (Yokogawa Electric Corp., Japan). Event-related synchronization was calculated at the source level using an optimal time-frequency beamformer (Dalal SS et al., 2008) with virtual sensors generated with 5mm voxels in the sphere space. Results from each subject were superimposed on an individual's brain MRI (3 T Philips and GEs MRI scanner). SERs were obtained from 49/56 hemispheres in the group of MCS patients, and from all of 102 hemispheres in the control group, respectively. Mean value of maximal frequency of oscillatory responses of SERs was 147 Hz for the MCS group, and 328 Hz in the healthy subjects group, respectively (unpaired two tailed t; $p<0.001$).The result support the previous study clarifying presence of abnormal somatosensory evoked responses in MCS patients (Iwasaki M et al., 2001) with a brand-new evidence from a standpoint of oscillatory neural activity.

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P1-060

MRC PARTNERSHIP GRANT: BUILDING CAPACITY IN UK CLINICAL MEG RESEARCH

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The UK MEG Partnership is a collaborative research programme between all eight UK MEG centres formed with the aim of building MEG clinical research capacity in the UK, and supported by a grant from the Medical Research Council (MRC). The partnership consists of Aston, Cambridge, Cardiff (lead administrator), Glasgow, Nottingham, Oxford, University College London and York. As well as supporting a cohort of PhD students and developing both unified training courses and common acquisition/analysis pipelines, a key research goal is to establish a normative database across sites. We aim to scan 80 individuals at each site to yield a total of 640 datasets, primarily comprised of healthy individuals. Standardised protocols involving a range of sensory localiser tasks, cognitive tasks and resting-state recordings will be established for this purpose, following a review of the current standards in clinical MEG. This characterisation of variability in a healthy cohort is required in order to make valid comparisons with clinical populations. The project will address the critical aim of research integration, and engender development of a principled approach to cross-site collaboration whereby it is possible to pool data from different scanner platforms, assess the reliability of measures and develop unified analyses. The process will also establish standards for future collaborations to ensure data is collected and

curated appropriately to enable data sharing and linking with other imaging modalities. Here we will describe 1) The UK MEG Partnership aims in detail, 2) The protocols and analysis strategies we will employ, 3) Our approach to unified training and collaboration and 4) Details of how the shared database will be created/curated and made available to the wider MEG community. If you are interested in the work of the partnership please contact either Bethany Routley (routleybc@cardiff.ac.uk - PhD candidate), or Krish Singh (singhkd@cardiff.ac.uk - lead principle investigator).

P1-061

INTERSESSION RELIABILITY FOR SOMATOSENSORY CORTEX LOCALIZATION: IMPLICATIONS FOR PRE-SURGICAL

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In patients undergoing neurosurgery for resection of a pathological area, pre-surgical planning often includes functional mapping to provide a detailed understanding of the brain topography. Magnetoencephalography (MEG) is used clinically to localize somatosensory cortex (S1) based on brain activity associated with median nerve stimulation. When utilizing this information, the surgical team needs to know the reliability of the localization provided by MEG. If the study was repeated, would the clinical team get the same answer? The intersession reliability of S1 localization with MEG has not been well established. The purpose of the current study was to quantify the intersession reliability of MEG S1 localization. Twenty healthy individuals underwent testing on 3 consecutive days. Each test comprised a series of 80 randomly ordered electrical stimuli to each median nerve at sub-motor thresholds. The somatosensory evoked field (SEF) pattern was used for localizing S1 in each session using an equivalent current dipole. The intersession reliability of SEF localization was determined based on the distance of each S1 localization from the average of the 3 sessions for each participant. The average distance from the mean localization was 2.2±0.4mm (95% confidence interval) along any axis. The average error using Euclidean distances was 4.8±0.5 mm. Thus, S1 localization is reliable between sessions to within half a centimetre. This result provides confidence for the clinical utility of single MEG scans to localize brain areas that are critical for somatosensation.

P1-062

AN EXPANDED RANGE OF APPLICATIONS FOR MEG THROUGH PERSONALIZED MEDICINE

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The advent of whole-head MEG systems has made possible to monitor the activity throughout the brain in real time, but it has not yet produced a revolution in the utilization of MEG in clinical practice. One of reasons may be the reliance on cryogenics and expensive shielding that limit real hospital environment utilization. Moreover, the brain activity revealed by real time tomographic analysis of whole head MEG data is too dynamic [1] with considerable variations, from subject to subject and from trial to trial within the same subject [2]. This view is very different from the long-held view established by the analysis of heavily pre-processed (e.g. filtering and averaging) EEG and MEG data. Recent clinical priorities have created the need for devices that can be widely accessible and under the control of individual patients at home. Although MEG cannot provide a complete personalized medicine solution as yet, it can play a key role in ensuring that cheaper devices are optimally designed to serve the needs of each individual patient. This approach has been at the heart of ARMOR, a project aiming to develop home-monitoring services for epileptic patients [3]. Traditionally, MEG epilepsy applications have emphasized pre-surgical evaluation. As ARMOR approaches its completion, its results point to new ways that MEG can contribute to epilepsy monitoring and management relevant to a wider population of epileptics. In fact, some of the methods developed are not only relevant to epilepsy but also open up wider commercial applications for MEG.

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P1-063

EFFECTS OF CONTRALATERAL NOISE ON THE 20-HZ AUDITORY STEADY STATE RESPONSE –MAGNETOENCEPHALOGRAPHIC STUDY–

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The auditory steady state response (ASSR) is an oscillatory activity of the brain, which is phase locked to the rhythm of an auditory stimulus. ASSRs have been recorded in response to a wide frequency range of modulation, but the physiological features of the ASSRs are somewhat different depending on the modulation frequency. Recently, the diagnostic importance of 20-Hz ASSR has been emphasized, especially in the area of psychiatry. However, little is known about the physiological properties of the 20-Hz ASSR, compared to those of the 40-Hz and 80-Hz ASSRs.

As for the effect of contralateral noise on the ASSR, it is known to depend on the modulation frequency to evoke ASSR. However, the effects of contralateral noise on the 20-Hz ASSR are not known.

In the present study, the effects of contralateral white noise were assessed on 20-Hz and 40-Hz ASSRs, using a helmet-shaped magnetoencephalography system in 9 healthy volunteers (8 males and 1 female, mean age 31.2 years). The ASSRs were elicited by monaural 1000 Hz long tone burst tone at 80 dB SPL, with the amplitude modulated at 20 and 39 Hz. The results indicated that contralateral noise caused significant suppression of both 20-Hz and 40-Hz ASSRs, although suppression was significantly smaller in 20-Hz ASSRs than in 40-Hz ASSRs. Moreover, significant right hemispheric predominance was only observed in 40-Hz ASSRs, despite the greatest suppression of both 20-Hz and 40-Hz ASSRs occurring in the right hemisphere when stimuli were presented to the right ear with contralateral noise.

The present study newly showed that 20-Hz ASSRs are suppressed by contralateral noise, which may be important both for characterization of the 20-Hz ASSR and for interpretation in clinical situations. Physicians must be aware that the 20-Hz ASSR is significantly suppressed by sound applied to the contralateral ear.

P1-064

BRAIN CONNECTIVITY MEASURES: APPLICATION TO EPILEPSY NETWORKS

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Introduction: Epilepsy is a neurological disorder that involves hyper exited brain regions that can be come overwhelmed leading to seizures. In Focal epilepsy these excited regions are in one location, which are ideal for a surgical resection. In Generalized epilepsy these excited regions can be found all around the brain. Understanding how functional brain networks send and receive information and how strong these networks are in patients with epilepsy may provide new avenues for future treatments as Generalized Epilepsy appears to be a network disorder. Recently we have shown that using Magnetoencephalography (MEG) coherence source imaging (CSI) to localize brain networks can provide a better outcome for temporal lobe epilepsy surgery. In the current study we expand the Connectivity measures to include Persistence and Granger Causality. Effective connectivity is the direct or indirect influence that one neural system exerts over another.

Method: An archival review of 57 presurgical MEG studies were performed. The MEG-CSI location, classified as Persistent, Sending and/or Receiving was determined from 10 min of spontaneous brain activity. This was compared to surgically resected brain areas. Engel outcome classifications were assessed using nonparametric tests.

Results: Comparisons of the patient groups for Engel classification showed significant differences in outcomes after resection of the receiver node of the network. Patients with any receiver resection had on average worse outcomes when compared to patients with no receiver resection. No significant differences were detected in outcomes for resections of the sender nodes or highly persistent brain regions.

Conclusions: We used MEG to determine the network properties in patients with epilepsy to identify the flow of information in the epileptic network. The MEG results from coherence source imaging (CSI) can provide information on the location of brain regions that are dominant and the direction and level of communication between brain regions.

P1-065

EVALUATING DEPRESSION SEVERITY BASED ON POSTERIOR ALPHA OSCILLATION

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In clinical practice, the diagnosis and treatment of depression are difficult, because the necessary information for an accurate decision on treatment strategy involves various aspects. Assessing recovery often relies on rating scales such as Hamilton Depression Rating Scale (HAM-D). Thus, the quality of the evaluation depends on the subjective ratings of the patient and the clinician. This study aims at developing a brain oscillations-based model that can help evaluating the depression severity. MEG brain activity was monitored while 24 medication-free patients diagnosed with major depressive disorder (MDD) and 24 healthy subjects viewed 3-s emotional videos. Strong and reliable posterior alpha (8-14Hz) modulations were found during the presentation of emotional facial expressions in both depressed patients and healthy controls. Regardless of emotional valiance, MDD showed consistently decreased posterior alpha activity compared to the controls, which might reflect that MDD had stronger emotional arousal in affective contexts. Accordingly, the modulation of posterior alpha oscillations were used to access whether a given participant had depression of by applying a logistic regression classifier. A discriminative performance (79.2%) was obtained using the data when happy stimuli were presented with leave one out validation. Moreover, the HAM-D score correlated with the posterior alpha power reduction when happy faces were shown. In conclusion, the present study suggests that altered posterior alpha activity may reflect emotion regulation abnormalities in MDD. Further the modulation of oscillatory activity in response to emotional faces is a useful approach to differentiate MDD from healthy controls. The proposed approach for distinguishing brain patterns may provide an objective research domain criteria improving the diagnosis and treatment of depression.

P1-066

DICOM COMPLIANT MEG LOCALIZATION INFORMATION INTEGRATION IN MRI STUDIES FOR ACCURATE IMPLANTABLE DEVICE SURGICAL PLANNING AND NAVIGATION

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Introduction: MEG localization of functional area for surgical interventions faces two challenges: different anatomical referential are used and both the implanted device and the surgical procedure have significant geometric constraints that have to be taken into account before generating a surgical planning. Commercially available neuro-navigation devices, while offering proprietary application programming interfaces (API) for multimodality data fusion lack MEG data handling, relying on sole DICOM import capabilities. We present a new method to introduce MEG functional localization data and implantable device characteristics as well as surgical parameters directly in DICOM compliant format with accuracy and safety checks to allow for surgical procedures guidance.

Materials and methods: Our method is based on transfer functions and a toolbox that allow:

- Multi-referential data and geometrical constraints representation with integrity check.
- After placement validation, visual representation and generation of virtual MRI slices with space sampling error minimization and control.
- Device constrained simulated ECoG with algorithm driven iterative electrode placement optimization.

Results: This clinical trial was approved by the ethics committee. We applied these methods to MEG recordings of imaginary motor tasks in 7 healthy subjects for BCI purposes. A BCI implant was defined as a 64 electrodes matrix. From simulated ECoG recordings, optimal electrode placement was automatically computed. Implantation constraints were fulfilled: a maximal cortex-implant distance of 0.5 mm, a bone thickness of more than 6 mm. The graphical information of the optimal drilling axis and its 50mm diameter as well as the electrode grid on the cortex allowed for a visual check of the feasibility of the intervention on the MRI. DICOM compliant slices were successfully transferred in a commercial neuro-navigation system.

Conclusion: We elaborated a cross-referential projection, calculation and simulation system with data integrity checking at all steps resulting in DICOM compliant series.

P1-067

FRONTO-PARIETAL ALPHA ACTIVITY REFLECTING VISUO-SPATIAL ATTENTION SWITCHING IS MODULATED BY DOPAMINE IN PARKINSON'S DISEASE.

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Alpha band activity has gained growing interest as a crucial mechanism for attention. As a consequence dysfunctions of this mechanism would cause cognitive deficits. Parkinson's Disease (PD) is known for its motor symptoms. However, a prominent cognitive symptom is a decrease in attention control. We studied the role of oscillatory alpha activity (8-12 Hz) in switching of attention. 20 Patients with PD, performed a visuo-spatial attention task. Patients had to attend to the left or the right visual hemifield, indicated by a cue. After a delay a visual stimulus was presented in both hemifields. A button press was required when the stimulus on the cued side changed color. MEG data (Elekta Neuromag, Vector View 306) and Unified Parkinson's Disease Rating Scale (UPDRS) scores were recorded a) after withdrawal of dopamine replacement medication (OFF) and b) after administration of L-dopa (ON). UPDRS-scores were significantly improved in the ON- compared to the OFF session ($p < 0.001$), assuring an effect of L-dopa administration. When patients had to switch the attended side between two subsequent trials compared to not switching ('normal switch-cost'), we observed a significant decrease in parietal alpha band activity. This effect was more strongly visible in OFF ($p = 0.009$) then in ON ($p = 0.059$). When patients had to switch the attended side after not switching the two previous trials ('increased switch-costs') the alpha decrease was even stronger (ON: $p < 0.001$; OFF: $p < 0.001$). Interestingly, with 'increased switch-costs' and only ON L-dopa, we observed an additional significant decrease of alpha band activity in frontal sensors ($p < 0.001$).These results indicate that decreased alpha band activity within the fronto-parietal attention network reflects an increased demand of resources and that this network is modulated by dopamine.

P1-068

DETECTING BRAIN CHANGES OF INDIVIDUAL TREATMENT EFFECTS DURING LANGUAGE THERAPY: A DOWN SYNDROME CASE STUDY

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Assessment of therapeutic treatment has relied mainly on behavioural testing using standardized tests. With the ready availability of non-invasive brain imaging technologies, there is increasing ability to integrate behavioural-based measures with brain-based assessments sensitive to individual treatment effects. We present case study magnetoencephalography (MEG) results for monitoring language therapy in Down syndrome (DS).

Behavioural data using the Peabody Picture Vocabulary Test 4th edition (PPVT-4) and functional brain data using MEG were collected during an 11-week language therapy session from a 9-year-old right-handed female participant with Down syndrome and normal hearing. Behavioural results showed a significant 21-point change between the pre- and post-PPVT-4 evaluations. MEG data were collected using a semantic violation paradigm that elicits the neuromagnetic equivalent to the N400, a response linked to the PPVT-4. Under condition of semantic violation this response shows an increase in amplitude around 400 ms between the incongruent compared to the congruent condition.

We outline a pipeline for analysis of changes at the individual level. The sensor-space MEG data across all datasets collected over the 11-week period were realigned to a common head coordinate space and independent component analysis was performed on the concatenated data. Cluster-mass permutation corrections were used to select components that showed sensitivity between the two conditions. A single component was identified that showed significantly larger amplitudes to the incongruent condition (p=0.027), consistent with a classic N400 response. This component showed a left lateralized topography. Comparison of this component across the 11-week period showed no significant differences in the congruent condition. However, there was a significant increase in magnitude in the incongruent condition (p=0.032) consistent with the behavioural performance data. The identified component demonstrated strong sensitivity to changes in semantic processing and provides initial demonstration for MEG monitoring in DS language therapy at the individual level.

P1-069
MEG-GUIDED PORTABLE MEDICAL DEVICE DEVELOPMENT: A PROOF-OF-CONCEPT

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To extend the diagnostic and therapeutic uses of MEG to facilitate more portable applications beyond the clinical setting, we are developing a translational model to determine the EEG correlates of MEG. By simultaneously recording MEG and EEG, we can exploit the spatial resolution of MEG to understand the specific activation signals in target regions such as the motor cortex. We can then link common signal changes between MEG and EEG, and "tune" these signals for point-of-care applications. Operationally, this means: 1) Identifying the participant specific portable (EEG-based) component of the MEG data, 2) verifying that the EEG component is actually representative of the paradigm under test, and 3) confirming this EEG component alone can provide brain function monitoring.

We conducted a pilot study by recording simultaneous M/EEG using a self-paced finger-tapping task with 20-second on/off blocks. Data were filtered from 7-35Hz and an independent component analysis (ICA) was performed. The ICA component of the MEG data with the most appropriate scalp topography (contra-lateral dipole location) as well as beta band power pattern (reduction during "tap blocks") was chosen. Similarly, ICA was also performed on the EEG data, and the ICA component with the highest cross correlation with the selected MEG ICA component chosen was selected as the linked EEG component. This was then verified using a combination of scalp topography as well as expected beta band power pattern.

Spatial source analyses confirmed the common neuroanatomical location across M/EEG. The successful proof-of-concept validation represents a first step towards the translation of MEG to more portable applications. Once the EEG component is identified and verified, it may be possible to utilize a portable low-cost device to monitor this specific brain function (ie, motor function recovery). These methods may also be extended to other functions/areas (eg, language processing).

P1-070
OSCILLATORY CORTICAL DYNAMICS OF IMPLICIT LEARNING IN PATIENTS WITH SCHIZOPHRENIA

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An emerging hypothesis in the neuropathology of schizophrenia is that alterations in oscillatory activity contribute to cognitive and behavioral symptoms prevalent in the disorder. More specifically, high frequency neural activity (e.g. gamma) is thought to be impoverished in the condition, with these deficits contributing to cognitive impairments found in this population. Here, we use magnetoencephalographic imaging (MEGI) to test the hypothesis that impoverished oscillatory activity over frontal cortices impedes implicit skill learning in schizophrenia. MEG data was collected using a 275-channel biomagnetometer (VSM MedTech) during a modified serial reaction time task (SRTT) using manual or vocal movements. Individuals were instructed to respond to a short vowel (/e/, /i/, /o/, /u/) presented in the auditory domain at the beginning of each trial. Subjects either responded by speaking the vowel they have heard (vocal), or pressing a button (manual) corresponding to one of four spatial locations. Stimuli were either presented randomly or in an eight-step movement sequence. Whole-brain oscillatory power changes were examined in the beta (12-30Hz), gamma (30-55Hz) and high gamma (65-115Hz) bands. Patients with schizophrenia failed to show learning effects for either response modality as a group (p>0.05) in comparison to healthy controls. Neurophysiologically, during the response phase, greater beta power suppression and increased high-gamma synchronization was observed when comparing the third sequence block to the final random block, and localized to bilateral dorsolateral and ventrolateral frontal cortex in healthy controls around movement onset. In patients with schizophrenia, this high-frequency oscillatory power over frontal cortex was not as robust as the patterns observed in controls over the same points in time. This data indicates that impairments in recruiting high-frequency neural synchrony translates into a deficit in cognitive learning at a rapid pace. These neuroimaging-based markers have the potential to track recovery following cognitive-based rehabilitative paradigms.

P1-071
EEG EVIDENCE OF STATISTICAL LEARNING IN PREVERBAL INFANTS

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Infants learn language rapidly and effortlessly, following a consistent developmental path, regardless of culture. The learning processes that are at play when learning from exposure are complex and multi-modal; however, a particular approach to language acquisition, called statistical learning, seems to account for a great deal of early speech structure acquisition. Statistical learning has already been shown to be a powerful implicit learning mechanism that infants can use to perform complex computations of co-occurrences among adjacent elements. In this study, using electroencephalography, we investigated infants' ability to compute statistical dependencies between more distant elements, and extract the underlying structure of a continuous speech stream. We also explored the interplay between experience and maturation, comparing 8-months-old full-term with preterm infants matched by maturational age or duration of exposure to speech. First, during a training session, infants were exposed to a 2 minutes continuous synthesized speech stream comprising AxC "words" separated by subliminal 25ms pauses. Then, during the subsequent test session, infants were presented with either "rule-words", that did not appear during training, but followed the training rule, or "part-words", that appeared in the stream, but violated the rule. Using frequency tagging to analyze the training, we found a significant power increase not only at the syllabic frequency but also at the word frequencies suggesting that infants were indeed parsing the stream into words. Rule learning was confirmed by the significantly different responses to "rule-words" and "part-words" around 550ms and 1400ms after word onset. These results, observed in the 3 groups together, suggest that long-distance dependencies are rapidly and easily used by infants to extract structural regularities in speech.

P1-072
FUNCTIONAL CONNECTIVITY AND ENTROPY MEASURES IN DEVELOPMENT

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As we mature, the brain becomes more adept at performing tasks, demonstrated through increased task performance and consistency, however the underlying neural correlates of development are less well understood. In this study we investigate both complexity (via entropy) and connectivity within multiple, well characterised brain networks, and how these effects change with age.

47 healthy volunteers aged 9 – 25 years took part. Subjects underwent a 5 minute resting state and two cognitive tasks, data recorded with a 275 channel CTF MEG system. Beamforming was used to reconstruct time-courses of source strength from large scale distributed networks (visual, motor, left and right fronto parietal networks). Canonical correlation analysis [1] was used to assess connectivity between two network nodes. Multiscale Sample Entropy (MSE) [2] was used to assess complexity within networks.

Functional connectivity was found to modulate significantly ($p<0.05$) with age, with reduced connectivity in younger participants. Effects were most pronounced in the motor network and left fronto-parietal network. Generally entropy was found to increase significantly ($p<0.05$) with age in all but the visual network, in agreement with [3]. MSE assesses entropy on multiple temporal scales; it was found that at short temporal scales entropy increases with age but at coarser temporal scales entropy decreased with age, thus highlighting the importance of high temporal resolution assessment.

Together these findings show that network dynamics, particularly in the fronto-parietal and motor networks, develop throughout adolescence, whereas the visual network dynamics appear stable from early childhood.

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P1-073
MEG CLASSIFICATION OF DEMENTIA BASED ON INCIDENTAL MEMORY TASKS.

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Alzheimer's Disease (AD) is the most common form of dementia, with around 4.6 million new cases diagnosed each year. The first signs of AD are typically problems with memory, which is a core feature of Mild Cognitive Impairment (MCI), a hypothetical prodromal state for AD. MCI is difficult to detect with conventional structural MRI images. Moreover, behavioural performance on clinical memory tests (like those used to define MCI) are affected by other factors like pre-morbid IQ, motivation, compensation strategies and self-awareness of memory problems. Functional neuroimaging of brain activity may therefore provide a more direct measure of memory, even when participants are not explicitly trying to remember, thereby by-passing many motivation/strategic confounds. MEG may be particularly useful in by-passing the potential vascular confounds of other functional measures like fMRI. However, memory tasks are needed that are 1) quick, 2) easy for patients with dementia and 3) independent of language (if to prove internationally useful). We therefore developed an incidental repetition paradigm, in which stimuli are repeated with lags of 9-20 seconds (beyond working memory), while participants respond only to rare target stimuli (that serve to maintain attention, but are ignored in analysis; i.e. no explicit memory task

is imposed). With this task, stimuli can be presented rapidly (every second), allowing approximately 200 initial and 300 repeated presentations of stimuli within 10mins. We tested two variants: one with simple repetition of scenes, and another in which a scene and object were repeated, but the location of the object within the scene was either switched or maintained. Both types of repetition tend to activate medial temporal lobe structures like the hippocampus using fMRI; the same structures that are affected in early stages of AD. We compared the ability of these MEG repetition effects to distinguish AD, MCI and age-matched control groups.

P1-074

THE NEURAL CORRELATES OF SPATIOTEMPORAL ORIENTING IN AGEING

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Knowing when events around us will happen is known to speed up action responses and improve perceptual processing. Recent evidence shows that this ability to orient attention in time declines with age. However, the neural mechanisms underlying this effect remain unclear. In the current study we looked at the neural correlates of temporal expectations in young and elderly participants to investigate the neural mechanisms that might be involved in the decline of temporal orienting effects in ageing. In this MEG study participants performed a covert spatiotemporal orienting task, which required a demanding perceptual discrimination. Cues were given on a trial-by-trial basis and indicated where (with 100% validity) and when (with 80% validity) targets would appear. The behavioral results show that in young participants, temporal expectations enhanced perceptual sensitivity and reduced reaction times to target events. Elderly participants, on the other hand, showed no significant improvement on accuracy or reaction times. The neural data were in line with the behavioral findings. In young participants, temporal information modulated the time course of lateralized anticipatory alpha desynchronization induced by the spatial cue. In elderly participants, preparatory alpha desynchronization related to the spatial cue was also present, but this effect was not significantly modulated by the temporal information also present in the cue. These results confirm that temporal orienting can be impaired in ageing. Furthermore, our findings suggest that while the modulation of alpha activity by spatial attention seemed to be intact, the ability to tune this anticipatory activity to relevant times was impaired. With ageing, we seem to lose the ability to direct our visual processing in time flexibly, which might be a more general process affecting other types of perceptual processing and the motor domain as well.

P1-075

ATYPICAL WORKING MEMORY BRAIN PROCESSES IN HIGH-FUNCTIONING CHILDREN WITH AUTISM SPECTRUM DISORDERS

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Working memory impairments may account for profound behavioural manifestations in children with autism spectrum disorders (ASD). Here we analyzed MEG (CTF, Omega-151) recordings while ASD and matched control children (20/group, mean age 11.25 years) performed an n-back task requiring to press a key when they identified the repetition of an abstract image presented 1 or 2 trials earlier. After MEG data preprocessing (band-pass filtering 1-70Hz, epoching -200:1200ms, baseline correction -200:0ms, head-movement(<5mm)/ICA artifact rejection) sources of MEG activity were localized using an event-related vector beamformer. Functional images of whole-head activity were generated for each condition (Repeat vs. New) and each memory load (1-, 2-back) by applying beamformer weights on averaged 50 ms time intervals over the task epoch of interest [0-600ms]. Although behavioural results were similar between groups (with all children performing above chance level), MEG sources for correct recognition effects (Repeat>New) were associated to atypical functional brain patterns in ASD both in the 1- and 2-back condition (all pcorr <.05). In the 1-back condition, correct recognition effects were associated with large and sustained activity of the right hippocampus and the right inferior frontal gyrus from 300 to 500 ms in controls while ASD recruited first the left dorsolateral prefrontal cortex from 200 to 300 ms followed by the insula bilaterally from 450 to 550 ms. Brain patterns associated with the 2-back condition also differed between groups. Although correct recognition effects revealed increased activity from 250 to 350 ms over the left insula and inferior parietal lobule in controls, these processes involved sustained activity of the left angular gyrus and the precuneus in ASD in this time window. These results suggest that specific brain functions involved in both low and high cognitive load of working memory processing are atypical in ASD, even in absence of obvious behavioural differences.

P1-076

ATYPICAL NEURAL ACTIVATION DURING AFFECTIVE PROCESSING IN CHILDREN WITH AUTISM SPECTRUM DISORDERS

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Emotional face processing is integral to successful social functioning, which is impaired in Autism Spectrum Disorder (ASD). The ability to perceive and interpret affective stimuli has an extended developmental course and is thought to reflect protracted maturation in neural areas implicated in affective processing. While atypical activation in key areas within the social brain network in response to facial affect has been reported in ASD, few studies have focused on investigating brain activity during childhood and the links between the neural activity and

social deficits observed in ASD. This study explored the temporal and spatial properties of MEG activation during implicit emotional face processing in children with and without ASD.

Twenty high functioning children with ASD (9M, 9.1+1.3 years) and 20 typically developing children (14M, 8.6+1.5 years) were tested. An emotional (happy or angry) face was presented on a monitor rapidly (80ms) and concurrently with a scrambled pattern (target) on either side of a central fixation cross. Participants indicated the location (right or left) of the target by pressing a button on a response box while fixating on the cross. Structural MRIs were obtained in all children for MEG data co-registration.

Emotion-related activation sources for each emotion were estimated using vector event-related beamforming. From 150-250ms, children with ASD showed significantly greater right superior orbital and superior temporal activation towards angry faces than controls. Children with ASD also showed greater right superior temporal activation towards happy faces, relative to controls, from 150-250ms.

While further data analyses are ongoing, our preliminary findings demonstrate differences in neural activity during affective processing exist in ASD in childhood and that these processes are continuing to mature. As orbital and temporal regions have been implicated in affective processing, investigating aberrant patterns of neural activity in these regions may aid in understanding atypical affective processing in ASD.

P1-077
REDUCED NETWORK CONNECTIVITY DYNAMICS IN PRETERM CHILDREN DURING VISUAL SHORT-TERM MEMORY PROCESSING

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Introduction: Children born very preterm display cognitive difficulties in domains such as visual spatial processing and executive functions. We used MEG to investigate changes in functional brain connectivity in this group during visual short-term memory (STM) processing.

Methods: 151-channel MEG (CTF) was recorded from 26 children born very preterm (≤32 weeks gestation, 7.7 years, 19 females) and 26 full-term controls (7.7, 17 females) performing a visual STM task. Dual state beamformer identified 39 regions with task-related activity in theta, alpha, beta and gamma bands. Inter-regional connectivity was estimated for a set of overlapping 0.5 s time windows using a two-source MPZ beamformer. Pairwise phase-locking value and weighted phase lag index were used to construct 39 x 39 connectivity matrices for each subject: one matrix per frequency band (B), time window (W) and connectivity measure (C). Then group averaged differential (preterm - control) connectivity matrices were calculated. BWC combinations showing multiple comparisons-corrected statistically significant group differences in connectivity ("significant BWCs") were identified.

Results: Significant BWCs were observed in all frequency bands. For each BWC, the sum of all elements of the differential connectivity matrix was negative, indicating reduced overall connectivity in the preterm group. Significant BWCs occurred most often in beta bands (12-16 and 16-24 Hz). They were found in 0.25 to 1 s interval relative to stimulus onset, and in 1.5 to 2 s interval at the end of the retention period. Preterms also showed smaller overall connectivity in the pre-stim interval in beta-bands. Location-wise, most differences occurred in connections involving left postcentral gyrus, right middle frontal gyrus, and right middle temporal gyrus.

Conclusions: Children born very preterm exhibit reduced functional connectivity during visual STM processing, indicating problems with neurophysiological network communication which may contribute to cognitive difficulties prevalent in this group.

P1-078
DISRUPTED BETA-BAND OSCILLATORY RESTING-STATE ACTIVITY IN ALZHEIMER'S DISEASE AND HEALTHY AGEING IN PARIETOFRONTAL AND SENSORIMOTOR NETWORKS

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Alzheimer's Disease (AD) is characterised by progressive dementia and increasing cognitive decline. AD is further associated with plaques and tangles, and grey and white matter atrophy; factors which severely affect the efficiency of neural communication. We investigated activity within well-known functional networks of oscillatory activity, a measure thought to be important for neural communication. We acquired MEG resting-state recordings from a group of AD patients, a group of well-matched elderly controls and a group of young controls. We used MEG independent component analysis to assess resting state network activity by calculating areas of high temporal correlation in oscillatory activity across the brain. We observed four prominent networks in the 13-30 Hz beta band: left and right parietofrontal, bilateral sensorimotor, and visual networks. Obtaining the standard deviation (SD) of component amplitude as a measure of (variability of) oscillatory activity within the boundaries of each network revealed that elderly controls had increased SDs compared to young controls in all networks except the visual network, whereas patients had decreased SDs compared to elderly controls in all networks. The differences in SDs were greatest and highly similar in the left and right parietofrontal networks, smaller in the sensorimotor network and weakest in the visual network. Interestingly, the SD values in the AD group were at a comparable level to that of the young control group. The pattern of SDs could not be explained by differences in head motion or positioning in the dewar or by beamformer weights. The findings suggest that elderly participants display greater variability in oscillatory functional networks, and that in AD this age-related variability is reduced. Speculatively, the reduced variability may reflect reduced neural communication, possibly related to atrophied white matter. The observed functional changes appeared strongest in more anterior networks, which may be related to cognitive deficits in AD.

P1-079

FACE PROCESSING IN PRE-SCHOOL AGED CHILDREN: A MEG NEUROIMAGING STUDY

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Introduction: It is still unknown whether the underlying mechanisms of face perception mature early or late in development. The current study examined this question by measuring face-specific brain responses (M170) from pre-schoolers using a paediatric MEG system. We also evaluated the effective connectivity of cortical networks underlying the M170; and compared the connectivity patterns of children to those of adults.

Methods: Fifteen children and 15 adults viewed pictures of faces, cars, as well as their phase-scrambled counterparts. Neuromagnetic brain responses were measured using a paediatric and a conventional adult MEG system housed in the same magnetically-shielded room. DCM analyses assumed that the M170 was mediated by sources in the lateral occipital cortex (LOC), mid fusiform gyrus (FG), and superior temporal sulcus (STS). Using Bayesian model selection, we evaluated three models of the interconnections between these regions.

Results: Face-sensitive M170 responses were obtained from both age groups. In the DCM analysis, the first and simplest model with only forward intra-hemispheric connections from LOC to FG and STS had the largest model evidence in adults, while in children, the second model with extra inter-hemispheric connections between LOC and contralateral FG showed the largest model evidence.

Conclusions: High-level face encoding mechanisms indexed by the M170 are present in children as young as 4 years of age; and the core face network underlying the M170 has a similar organization in children and adults. However, the functional organisation of the core face network undergoes further development and fine-tuning before it reaches adult capacities.

P1-080

LATENCY OF PRIMARY SENSORY RESPONSES TO MULTISENSORY STIMULI IN ADOLESCENTS WITH AND WITHOUT FETAL ALCOHOL SPECTRUM DISORDERS (FASD): EFFECTS OF SPATIAL CONGRUENCE

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Spatially congruent multisensory stimuli are known to elicit larger amplitude electrophysiological responses in subcortical and primary sensory areas compared to incongruent multisensory stimuli, or unisensory stimuli alone; however, the latency effects of spatial congruence between auditory and tactile stimuli in humans have not been studied. Here, we studied the effects of auditory and tactile stimulus congruence on primary auditory and somatosensory response latency in adolescents (12-21 yrs) characterized as having an FASD (N=18) and age-matched healthy controls (N=22), using Magnetoencephalography (MEG; Elekta Neuromag). Unisensory auditory/tactile and simultaneous spatially congruent/incongruent multisensory stimuli were presented while participants watched a silent cartoon. We first projected noise from the raw data and performed motion correction using Neuromag Maxfilter. Heartbeat and eyeblink artifacts were then projected from the data using signal space projection before averaging and source localization. Source analysis was performed using the Cortical-Start Spatio-Temporal (CSST) multi-dipole analysis method available in MRIVIEW. The MEG data were registered to the individual subject MRIs for source analysis and visualization purposes. We analyzed the timecourse of activity for cortical sources localized to primary auditory and primary somatosensory cortices, and found a significant delay in latency of the first three prominent peaks (M50, M100, & M200) in the auditory evoked source activity for FASD relative to HC (all p's < 0.05). Also, a double dissociation was found for the effect of multisensory congruence on right hemisphere primary auditory and primary somatosensory response latencies for HC vs. FASD ($p < 0.001$). These results are consistent with animal literature and previous results from our lab demonstrating a delay in basic visual and auditory processing, as well as studies showing structural and functional deficits specific to the right hemisphere in FASD.

P1-081

INTRINSIC ALPHA-BAND FUNCTIONAL CONNECTIVITY IN THE ATTENTIONAL DORSAL VISUAL NETWORK IN CHILDREN

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The developing brain might be viewed as a dynamic system of relationships between intrinsic oscillating networks. The intrinsic or resting state fMRI signal has been used to show age-dependent changes in functional connectivity. However, since the developmental phenomena are tightly linked to time, high-temporal resolution MEG and EEG will improve understanding development of functional connectivity (fcMEG, fcEEG). We focus on the frontal-parietal, attentional dorsal visual network (ADVN) involving anatomically-defined superior frontal and inferior parietal nodes, and on the related alpha-band oscillatory activity (8-13 Hz). ADVN plays a prominent role in inhibitory control of cortical excitability, cognitive development and child psychopathology. We pose important question, whether ADVN matures early or shows protracted maturation, such as the frontal-striatal network. Our earlier studies on task-evoked MEG alpha-band connectivity suggest that ADVN's intrinsic alpha-band connectivity will display early maturation, thus, no significant child-adult differences will be seen in intrinsic alpha-band fcMEG and fcEEG. Methods: Intrinsic alpha-band was recorded (3x4 min during resting with rigorous motor control) from 12 children (age 7-15) and 12 adults (age 21-42) using MEG (VectorviewTM, Elekta Neuromag, 306 sensors) and EEG (64 Channels BIOSEMI). Computing included: fcMEG using the imaginary coherence, 30sec alpha-band time windows;

fcEEG alpha-power using custom script EEGLAB; average alpha coherence (30sec) in regional clusters using Mscohere, MATLAB; statistical comparison of amplitudes and coherence between nodes by group (children vs. adults). Results: no significant group contrasts in strength fcMEG coherence between homologous nodes of the parietal cortex and right frontal-parietal connectivity; other measures were different between children and adults (p< .01); fcEEG alpha power is higher (.005) and fcEEG coherence is lower in children(.01). These findings support in part early maturation of ADVN but stand in contrast to findings on task-evoked MEG functional connectivity. Conclusion: Task-evoked and resting-state functional connectivity may indicate different developmental neural phenomena.

P1-082

DEVELOPMENT OF SUPERIOR TEMPORAL GYRUS 40 HZ AUDITORY STEADY-STATE RESPONSES IN TYPICALLY DEVELOPING CHILDREN AND CHILDREN WITH AUTISM SPECTRUM DISORDER

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Background: Theories of brain abnormalities in autism spectrum disorder (ASD) often posit a central role for gamma (~40Hz). In adults, tones amplitude-modulated at 40Hz are often used to assess the integrity of superior temporal gyrus (STG) gamma-band circuits. Studies, however, suggest that 40Hz auditory steady-state responses (ASSRs) are not fully developed in children. To further explore this issue, left and right 40 Hz ASSRs in typically developing (TD) children as well as in children with ASD were measured.

Methods: MEG data were obtained from fifty-two TD children (49males; 6-14years) and forty children with ASD (36males; 8-14years). 40Hz amplitude-modulated tones of 1sec duration (5sec ISI) were binaurally presented. T1-weighted structural MRI was obtained for magnetic source analysis. Left and right STG gamma evoked activity was modeled (300-950ms) using single dipoles, and left- and right-hemisphere 40Hz total power (TP) and inter-trial coherence (ITC) measures were obtained.

Results: Hierarchical regressions showed in TD and ASD an association with age and 40Hz ASSR ITC bilaterally (p<0.01). The interaction term was not significant, indicating in both groups a ~0.01/year increase in ITC. 40Hz TP was not associated with age in either group (p>0.05). The TD and ASD groups did not differ in 40Hz TP or ITC.

Conclusions: An age-related increase in 40Hz ITC but not TP indicated that the STG 40Hz ASSR develops primarily as a result of an increase in neural synchrony. Given a ~0.01/year increase in ITC values, adult-like 40Hz ASSRs were not observed until late adolescence. Although STG 40 Hz ASSRs were very weak in young children, present findings indicated normal development of STG 40Hz ASSRs in children with ASD.

P1-083

OSCILLATIONS, NETWORKS AND THEIR DEVELOPMENT: MEG AMPLITUDE CORRELATIONS IN RESTING-STATE NETWORKS STRENGTHEN WITH AGE

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Magnetoencephalographic (MEG) investigations of inter-regional amplitude correlations have yielded new insights into the organization and neurophysiology of resting-state networks (RSNs) first identified using fMRI. Inter-regional MEG amplitude correlations in adult RSNs have been shown to be most prominent in alpha and beta frequency ranges and to express strong congruence with RSN topologies found using fMRI. Despite such advances, little is known on how oscillatory connectivity in RSNs develops throughout childhood and adolescence. The present study used a novel fMRI-guided MEG approach to investigate the maturation of resting-state amplitude correlations in physiologically relevant frequency ranges within and among six RSNs in 59 participants, aged 6-34 years. We report age-related increases in inter-regional amplitude correlations that were largest in alpha and beta frequency bands. In contrast to fMRI reports, these changes were observed both within and between the various RSNs analyzed. Our results provide the first evidence of developmental changes in spontaneous neurophysiological connectivity in source-resolved RSNs, which indicate increasing integration within and among intrinsic functional brain networks throughout childhood, adolescence and early adulthood.

P1-084

PERFORMANCE EVALUATION OF A NOVEL PEDIATRIC MEG SYSTEM

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We used simulations to evaluate the performance of the "BabyMEG" magnetoencephalography (MEG) system, which is designed for pediatric populations and is becoming operational at Boston Children's Hospital. The BabyMEG system features a unique two-layer sensor array with 270 and 105 superconducting quantum interference device (SQUID) magnetometers in the inner-and outer layers, respectively. The helmet is designed for children up to 5 years of age. This enables the sensors to be located as close 15 mm from the cortex, which is more than two times closer than in conventional MEG systems. The closer distance increases the signal-to-noise ratio and enables the system to acquire higher spatial frequencies of the magnetic field patterns, which drastically improves the source localization accuracy and resolution of simultaneously active multiple sources. We performed simulations to compare the BabyMEG system with the Elekta Neuromag Vector View MEG system as well as with high-density EEG systems. The simulations were conducted in a realistic three-layer boundary-element model. We evaluated the dipole localization accuracy for

extended sources and single dipoles over the cortex. We also evaluated the performance in terms of point spread for minimum-norm (MNE) source localization methods. Finally, we computed the information-theoretic channel capacity, which is a measure that quantifies the amount of information that can be gained from the brain under realistic noise conditions. Our results clearly demonstrate the superiority of the BabyMEG system, i.e., it offers a significantly better dipole localization accuracy, especially for deep sources or locations where the dipoles are close to being radially oriented, reduced point spread in MNE methods, and an increased channel capacity. The results show that the BabyMEG system is uniquely suited to study disorders such as epilepsy, where it is necessary to map the neurophysiological activity in the brain with a high spatio-temporal resolution.

P1-085
MU RHYTHM SUPPRESSION IN TERM AND PRETERM INFANTS

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Infants born prematurely are at increased risk for long-term cognitive delays or impairments relative to healthy term infants. Surprisingly, medical course during the immediate post-natal period does not provide good predictive power as to which infants will go on to experience long-term impairments. Furthermore, behavioral assessments at young ages also do not provide sufficient sensitivity to determine the children at highest risk. Therefore, we assessed preterm infants (<29 weeks gestational age) with an uncomplicated course (Grade I or II intraventricular hemorrhage, no history of seizures, no indication of cerebral palsy) at 3 & 6 months corrected age relative to healthy full-term infants. The sensorimotor system is one of the earliest systems to develop in infants and is important for both motor execution and imitation abilities. We therefore, measured the responsiveness of the sensorimotor resting mu rhythm using MEG during an imitation and resting task. The infants also underwent developmental assessment using the Bayley Scales of Infant Development III (BSID-III). The preterm infants at 3 months of age had significantly lower cognitive scores on the BSID-III relative to the term infants. A pattern of mu rhythm suppression was observed across groups with greatest mu power during rest and mu rhythm suppression during infant squeeze conditions. Furthermore, the frequency of the second harmonic of the mu rhythm was significantly greater in preterm infants relative to term infants. In light of our previous results indicating a linear increase in mu rhythm frequency in healthy term infants 0-12 months of age, the current results suggest that the preterm infants' sensorimotor mu rhythm may be more developmentally advanced relative to term infants. This result is contrary to our hypothesis that mu rhythm development would be delayed in preterm relative to term infants and may be associated with their preterm birth.

P1-086
NEUROMAGNETIC OSCILLATIONS IN WORKING MEMORY PROCESSES

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Brain injuries as well as changes in white matter integrity during ageing reduce the effectivity in neural communication. In both cases, working memory performance is impaired. Functionally relevant neuromagnetic activity may serve as a biomarker for diagnosing and monitoring therapeutic intervention.

A modified Sternberg paradigm was used for studying memory for items at different positions in a study list. MEG was recorded with a 151-channel system while participants studied a sequence of five visually presented letters. They decided if a pair of probe letters had been presented in same order or reverse order in the study list. Time-frequency analysis was applied to the MEG sensor data. Partial least-square (PLS) analysis identified spectro-temporal components and spatial distributions of neuromagnetic oscillations related to task difficulty and performance.

Reaction times (RT) were longer for the reverse ordered probe indicating higher task load compared to the same-order probe. RT increased with the serial position in the study list with the exception of shorter RT for the last position indicating a recency effect.

Alpha and beta oscillations showed event related desynchronization (ERD) following the visual stimuli during the encoding interval and after probe presentation. Theta oscillations showed event related synchronization (ERS) most prominently in fronto-temporal sensors.

The magnitudes of alpha and beta ERD increased with the serial position of items during encoding and were stronger for the more difficulty task of identifying the reverse ordered probe. PLS identified spatio-temporal factors of alpha and beta ERD that showed same dependency on serial position and probe order as RT and were correlated with RT. Retrospective PLS analysis showed stronger alpha and beta ERD during the encoding interval for the correctly remembered probes compared to forgotten items. The identified spectro-temporal modulations will be used for study task and performance dependent changes in functional connectivity.

P1-087
FUNCTIONAL SIGNIFICANCE OF BETA- AND GAMMA- BAND NEUROMAGNETIC OSCILLATION AND PLASTIC REORGANIZATION AFTER MUSIC TRAINING IN AGING

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Music, or rhythmic sounds, facilitate synchronized body movements even in Parkinson's disease (PD) patients with motor impairment off-medication. In healthy adults, best synchronization occurs with a tempo of around 600

ms onset-to-onset, coinciding with the optimal perception of musical beat. However, physiological mechanisms underlying auditory-motor coupling remain unknown. Beta-band oscillation is deeply associated with somatomotor systems. Our previous study using magnetoencephalography (MEG) indicates that timing of isochronous sound is reflected in the endogenous broad-band response in the auditory cortices. Furthermore, gamma-band (~40Hz) neural oscillations are considered to reflect neural computation for object feature binding and memory processes. In our previous study, gamma-band increase was evident even after the occasional stimulus omission, indicating anticipatory processing. Here we investigated how auditory and somatosensory information are interacting in beta-band and gamma-band, and how music training affects these neural networks in the healthy elderly. Specifically we asked the questions; (1) Does beta-band oscillation play a role in linking auditory and motor systems during listening to rhythmic sound in the absence of a motor task? (2) How does music training affect beta- and gamma-band oscillatory somatomotor network? 6 healthy older adults received piano lessons for 5 weeks whereas another 6 had no training between pre and post training MEG recording. MEG was recorded with 20-Hz vibro-tactile pulse trains delivered on the tip of index finger (D2) in one block and on the ring finger (D4) in another block, also in listening to isochronous auditory stimuli (e.g., metronome). Only gamma-band response showed a significant amplitude increase in piano-training group. Gamma-band network may link auditory-somato-motor integration. Moreover, listening to isochronous auditory stimulus activated beta-band oscillatory networks similarly to those in young adults. The results suggest that beta and gamma-band oscillations are differently used for supporting auditory-motor coupling, and useful biomakers for the training-induced plasticity.

P1-088

BRIDGING THE GAP IN THE NEUROIMAGING OF EARLY MOTOR DEVELOPMENT: EVIDENCE FROM MEG STUDIES IN PRESCHOOL AGE CHILDREN

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We recently reported the first recordings of movement-related brain activity in preschool age children using a custom-sized pediatric MEG system (Cheyne et al., in press). A videogame-like task was used to generate self-initiated right or left index finger movements in seventeen healthy right-handed preschool age children (8 female, ages 3.2 to 4.8 years). Using beamformer source analysis and a surrogate MRI normalization procedure, we demonstrated that motor fields and movement-evoked fields demonstrated different timing and polarity in comparison to adults, as well as the timing and frequency of movement induced oscillatory activity, with greater co-modulation of mu and beta rhythms at lower frequencies. We also observed transient high-frequency gamma oscillations in motor cortex at movement onset, similar to that observed in adults, but with some children also showing bursts in the lower gamma range. We report here initial results from a two-year follow-up study in the same children where some demonstrated signs of a shift towards more adult-typical patterns, including earlier MEFI peak latencies and polarity. Interestingly, we also detected changes in the peak frequency of movement induced gamma oscillations. These findings provide additional evidence that basic sensorimotor activation patterns are markedly different in children prior to 5 years of age, and undergo maturational changes from early to later childhood. Such changes have implications for both early brain development and our understanding of its role in normal and abnormal cognitive development.

P1-089

GROUP ANALYSES OF MULTIVARIATE DECODING METHODS IN MEG

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The brain encodes exteroceptive and proprioceptive information into complex patterns, which can be observed across multiple dimensions of MEG data. Improving upon traditional, mass univariate analyses, multivariate supervised learning algorithms capture these complex patterns encoded across time, space, and frequency simultaneously. Here, we use machine learning algorithms to investigate multivariate MEG patterns in space and frequency that decode for different visual stimuli, which engage distributed, yet distinct, networks across multiple subjects. MEG (306-channel Elekta Neuromag) data was obtained from 14 healthy participants who were presented with a sequence of images of either emotional faces or motorbikes. The input feature space spanned multivariate spatial and spectral information for each time point, with target classification labels of faces or motorbikes. Machine learning algorithms were trained, tested, and validated to assess each for classification accuracy and uncertainty. The algorithms implemented included: Naïve Bayes, support vector machine, decision tree, random forest, and logistic regression. Sensor space results were beamformed into source space to investigate the spatial distribution of classification information across the brain. Results were combined over multiple subjects by feeding subject-level statistics to group-level binomial testing. Initial above-chance significant classification findings replicated previous wideband (5-40 Hz) results on the same dataset using a traditional mass univariate analysis pipeline. The feature selection and feature ranking techniques implemented here allowed for multivariate investigation of complex patterns offering additional useful information for classification. Furthermore, this work extends subject-level results to formal group-level multivariate classification using higher order statistics. By implementing basic machine learning algorithms to analyze MEG data at the group level, we offer a novel method of incorporating multivariate spatial and spectral information to drive data exploration. These techniques are early steps towards understanding the complex interactions observed in brain activity.

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P1-090

NEUROFEEDBACK FOR HAND THERAPY AFTER PARALYSIS USING REAL-TIME MAGNETOENCEPHALOGRAPHY

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By providing neurofeedback, individuals can learn to volitionally modulate their cortical activity which may induce plasticity and could impart therapeutic benefits (e.g. strengthening corticospinal pathways for improved motor function). Magnetoencephalography (MEG) can be used to provide this neurofeedback for rehabilitation applications and to assess neuroplasticity associated with therapy.

Real-time feedback of hand-related sensorimotor rhythms was provided to 8 individuals with tetraplegia. The spectral power over the contralateral sensorimotor cortex was assessed every 50ms and used to control the aperture of a virtual hand. After ~5 minutes of open-loop data collection, subjects performed up to 200 brain-control trials which required proportionally moving a virtual hand to an open-or-close target. Task difficulty was adjusted to encourage plasticity by increasing the required hold time to maintain a success rate between 50 and 75%.

Participants reached successful targets with a 500ms hold time in 1.94±0.39 (mean±sd) while maintaining a 57±13% success rate. Four subjects who participated in a follow-up session one week later showed similar performance with small decrease in success rate (3±7%) and increase in time to target (slowed by 0.11±0.28s). However, from the last 40 trials of session one to the first 40 of session two a 9±8% increase in success rate was found suggesting participants had retained the ability to perform the task.

We have shown that individuals with paralysis can gain control over MEG-based neurofeedback. We are now investigating the effect of neurofeedback on sensorimotor cortex activity as well as hand function.

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P1-091

ROLES OF SENSORY INFORMATION IN CONTINUOUS DECODING OF ARM MOVEMENTS FROM MEG CORTICAL SOURCES

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The aim of this brain-computer interface (BCI) study is to provide the ability to control external devices to severely disabled people. Although the sensory information is known to be important for accurate goal-directed movements, it remains unclear what roles sensory information plays in the decoding of continuous movements. In this study, we aim to investigate contribution of sensory information in decoding continuous movements by reconstructing source activities and then investigating the effect of visual feedback in continuous movements decoding.

A whole-head 306-channel system was used for MEG recording. Nine right-handed healthy subjects were instructed to draw a circle and a diamond with or without visual feedback. A cursor represented the current arm position, and was not shown for the condition without visual feedback. We selected ROIs known to be relevant for motion control, which consisted of the premotor cortex, supplementary motor area, primary motor cortex, intraparietal sulcus and parieto-occipital sulcus. Source time-series were then estimated for each ROI using beamformer analysis. The arm positions were continuously decoded by the multiple linear regression method using 2Hz low-pass filtered signals from all ROIs, or each ROI.

The correlation coefficients (CCs) between measured and decoded position profiles were not significantly different between decoding results across source signal from each ROI. This result shows that the sensory-related areas are equally as important as motor regions for decoding continuous movements. The CC of conditions without visual feedback was significantly lower than the condition with visual feedback. There w was an effect of visual feedback in decoding movements, but decoding accuracy was still high even when visual feedback was absent. This implies that proprioceptive feedback might be also play an important role in decoding continuous movements.

P1-092

ABSTRACT AUDITORY CATEGORICAL REPRESENTATIONS AND DOMAIN-GENERAL DECISION MAKING: A MULTIVARIATE MEG STUDY

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The ability to distinguish between different classes of objects and incorporate them into discrete categories is at the basis of cognitive functioning and is fundamental for survival and everyday life. Perceptual and categorical decisions make sense of our reality and allow us to interact with the world. Deciding into which category a stimulus falls must be done effortlessly, regardless of how it is perceived or whether it requires a response or not.

Studies have shown that motor programs are prepared concurrently and pre-eminently characterize the perceptual decision process and the accumulation and integration of the sensory evidences needed to make a choice (Gold & Shadlen, 2003). This has led to the development of an intentional framework stating that decision making happens in the very same sensory-motor cortex where the response associated with the decision is prepared (Shadlen et al., 2008). However, more recent research, suggesting a more intuitive perceptual- and motor-invariant decision-making module, has put this theory into question (Freedman & Assad, 2006, 2011).

In order to examine the perceptual decision process, abstracted from sensory and motor influences, a delayed-match-to-category task using auditory stimuli was presented to participants while they were scanned using

magnetoencephalography (MEG).

The use of a cognitive set and a delayed response to report the choice can disentangle decision-making from motor planning and execution. Two difficulty levels produced by manipulating fast and slow frequency modulations (individually determined using adaptive procedures) helped to separate decision variables modulation. Auditory stimuli with two different base frequencies (i.e. tone pitch) allowed to separate higher-level categorical signal from primary perceptual discrimination. Since the univariate analyses were not informative and hardly reached significance, a multivariate approach (Oosterhof, 2013) was proposed in order to uncover patterns of activity containing abstract categorical information beyond low-level perceptual differences from cortical oscillatory activity.

P1-093

EVALUATING MACHINE LEARNING TECHNIQUES FOR OPTIMIZING MOTOR IMAGERY NEUROFEEDBACK

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Functional recovery post-stroke depends on therapies that can effectively drive neural plasticity in patients with highly variable capabilities. Motor imagery (MI) is one therapy that can promote recovery of motor function even in a paretic limb. When coupled with neurofeedback (i.e., real-time displays of neural activity), both patients and clinicians can monitor MI performance and efficacy, and MI effectiveness may be improved. However, it is unclear which brain signals should be utilized for the provision of optimal neurofeedback. Intelligently identifying the signal components which best represent MI in each patient may improve the quality of neurofeedback, and therefore MI interventions.

In this study we evaluate the effectiveness of machine learning algorithms, which generate predictive models from high dimensionality data, for (1) accurately classifying MI activity and (2) identifying the characteristics of magnetoencephalography-based (MEG) signals that are most strongly indicative of MI. Machine learning was applied to MEG-based virtual sources in each primary motor cortex of 20 non-disabled participants during rest, actual performance of a skilled motor task (motor), and MI. The machine learning model was trained and tested on classifying data segments from all participants using 10-fold cross-validation, with model parameters selected by stochastic search where appropriate.

Classification accuracy between motor and rest data segments ranged from 95% to 74%. Between MI and rest segments, accuracy ranged from 94% to 66%. Examination of the weights showed discrimination was primarily based on left hemispheric activation in the 20-30 Hz band for motor blocks, and 30-40 Hz bilateral activation for MI. Ongoing extensions of this research include the use of additional virtual sources at the regions of interest outside of the motor cortex, and the use of neurally inspired models (Restricted Boltzmann Machines, Cortical Learning Algorithm) with superior reconstruction and classification ability.

P1-094

HIGH-PERFORMANCE BRAIN MACHINE INTERFACE COMBINING IMAGE INFORMATION

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Introduction: The brain–machine interface (BMI) technology has been used to restore motor functions of the patients. However, the accuracy of controlling a robotic arm was quite low (Hochberg et al., 2012). One of possible reasons for the low accuracy is that previous BMI studies have not considered sensory feedback to predict movements (Hochberg et al., 2012; Collinger et al., 2013). Here, we propose a novel prediction method, the feedback-prediction algorithm (FPA), to generate feedback information from the positions of objects and using the feedback to predict movements.

Methods: We recorded MEG signals from 9 healthy subjects. During the MEG acquisition, subjects were instructed to move their arm according to the 3D center-out-and-back task. To predict the movements, we used the same features as described previously (Yeom et al., 2013). We predicted the 3D arm movements from the MEG signals in both cases with feedback (FPA) and without feedback. The proposed FPA modifies the predicted direction toward the target and modulates the magnitude of the predicted vector to easily reach the target by combining feedback information.

Results: The accuracy of the movement prediction was significantly improved for all subjects ($P < 0.001$) and 32.1% of the mean error was reduced by combining feedback information (FPA). The results demonstrate that the end points of the trajectory predicted with the feedback were closer to the target and also more focused on the target than the end points predicted without feedback.

Conclusions: We demonstrated that combining feedback information for movement prediction considerably improves prediction accuracy. The proposed method will improve the performance of the arm-control BMI system not only for non-invasive but also for invasive brain signals. Therefore, the FPA will promote the development of a practical BMI system.

P1-095

MEG DECODING ACROSS SUBJECTS

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Predicting the mental state of a subject from concurrent neuroimaging data is a data analysis approach called brain decoding. An accurate decoding model provides evidence for the existence of stimulus-related information in the recorded brain data, a conclusion that sheds light on the relation between the mental process of interest and its neural correlates. Recently, this approach has attracted researchers in neuroscience where it is used as a quantitative method to test hypotheses on neuroimaging data.

Brain decoding is generally applied at the single-subject level and inference at the group-level is commonly achieved by aggregating the single-subject results. An alternative solution to make inference at the group level, called decoding across subjects, is to train a classifier on the trials of a group of subjects and then to test it on unseen trials from new subjects. But the structural and functional variability across subjects, together with systematic differences in measurements across different acquisition sessions, make the decoding across subjects extremely difficult.

In this study, we formulate the problem of decoding across subjects from magnetoencephalographic (MEG) data as an instance of transductive transfer learning (TTL). Transfer learning aims at transferring knowledge from the train set to the test set, assuming they differ in some aspects. As a further contribution, we present a simple and practical TTL solution based on the covariate shift assumption. Our final contribution is the use of an ensemble learning technique, called stacked generalization, to enhance the training process of the classifier on the data from different subjects. On a face vs. scramble MEG dataset of 16 subjects, we compare the standard approach of not modeling the differences across subjects, to the proposed one of combining TTL and ensemble learning. We show that the proposed approach is consistently more accurate than the standard one.

P1-096

INFORMATIVE TIMING DETECTION IN A TRIAL-BY-TRIAL MEG DECODING FRAMEWORK

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In this work we present a new MEG decoding framework, which includes several main building blocks: 1) Features extraction methods for the MEG recordings, 2) Channels selection model, 3) Trial by trial prediction using a support vector machine (SVM) classifier, 4) Hyper-parameters grid search for the classifier and the channels-selection models, 5) Intervals selection over the time domain, 6) Prediction accuracy calculation over sliding windows, and 7) Detection of significant informative time windows.

We tested the framework on recordings from an auditory task, where the subjects needed to identify whether a specific melody's scale is major or minor. The melodies' scale can be identified only in the third note. We tested two binary classifiers: third notes vs second notes, and third notes vs random notes. In the results we show that using our platform one can identify between the different cases without the need to average the subjects' responses, and that the informative timings correlate with the subjects' behavioral results. Moreover, by detecting the significant informative time windows in each trial we were able to identify the specific neural activity for a melody scale recognition.

P1-097

DECODING MOTOR INTENTIONS USING PHASE, AMPLITUDE AND PHASE-AMPLITUDE COUPLING

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Intracranial EEG (iEEG) recordings from the human motor cortex can be used to infer movement parameters such as limb movement direction or kinematics. While most decoding studies rely on spectral power in specific bands, there is a growing interest in the potential utility of cross-frequency measures, such as Phase-Amplitude Coupling (PAC) as a new promising neural feature to decode movement plans. Here, we investigate the feasibility of using three features of neuronal oscillations, phase, amplitude and PAC to classify movement-related states (Rest vs. Planning vs. Execution) and movement directions (prior to and during execution). To this end, several subjects implanted with iEEG electrodes in multiple brain structures performed a delayed center-out motor task (up, down, right or left). We used Hilbert transform to extract the instantaneous phase and amplitude in multiple frequency bands and to compute various PAC measures. We first evaluated the performance of each type of feature separately. Then we tested whether combining both features could further improve the decoding accuracy (DA). The prediction accuracy of the various features was estimated using linear discriminant analysis and cross-validation and multi-feature selection was based on a forward selection procedure. Our findings demonstrate that, combining phase, amplitude and PAC features in multiple frequencies bands and brain structures provides significant classification performances for motor states discrimination and high movement direction prediction not only during execution, but even during action planning. Generally, our findings suggest that broadband gamma (60-250 Hz) power and its coupling with the phase of lower frequencies such as delta (2-4 Hz), theta (4-8 Hz) and alpha (8-12 Hz) provide the highest decoding performance. The ability to decode movement intentions prior to movement execution may have interesting implications for the development of novel brain-computer interface strategies.

P1-098

AUTOMATED MODEL SELECTION FOR SPATIAL WHITENING AND COVARIANCE ESTIMATION OF M/EEG SIGNALS

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The estimation of the spatial covariance of the brain signal and the related noise structure is a fundamental building block of modern M/EEG data analysis pipelines. Such covariance estimates are commonly used in all source localization methods for spatial whitening and data covariance estimation,

and hence, critically determine the success of the analysis. While maximum likelihood estimation leads to a covariance estimate known as empirical covariance, since it is estimated on a limited number of data, it turns out to be a rather poor estimate of the true covariance. The most common approach pursued to alleviate this problem consists in down-weighting off-¬diagonal coefficients. More advanced methods are based on generative models, such as probabilistic Principal Component Analysis (PPCA), Factor Analysis (FA) or shrinkage approaches. Here we propose an automated model selection procedure based on Gaussian likelihood and cross-¬validation. To compare the properties of the covariance estimators, we considered four different simulation scenarios representing a 2 (homoscedastic VS heteroscedastic noise) X 2 (low VS high rank) grid. For each cell in this grid rank estimates were computed for PPCA, the Bayes PCA criterion and FA with a continuously increasing number of samples. In a second step, model likelihood was computed for the Ledoit-¬Wolf and the SC estimator as well as for PPCA and FA. Subsequently, the covariance and rank estimation procedures were tested using M/EEG data recorded on three widely used MEG systems: a 4D-/BTi Magnes-3600WH, a VSM MedTech Inc. / CTF, and, a Neuromag VectorView system. Our results demonstrate that, depending on the data, the optimal whitening operator can be computed based any covariance model. The proposed automatic model selection should therefore help leveraging reproducible research.

P2-001

MOTOR ORIGIN OF TEMPORAL PREDICTIONS IN AUDITORY PERCEPTION

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Predicting not only what could happen, but also when it could happen bears significant advantages for selecting relevant sensory signals in a noisy environment. It is proposed that low-frequency oscillations are the substrate of temporal predictions. At the sensory level they modulate the excitability of neural populations of interest to optimize sensory selection. However, where such top-down signals originate is currently unknown. We hypothesized that the motor system generates temporal predictions in the form of slow oscillations, and optimizes sensory processing via the dorsal 'what/when' parietal stream. We developed an auditory task of temporal attention, to specifically track temporal prediction neural signals (recorded with magnetoencephalography) and observe their behavioral influence. We provide evidence that the motor cortex acts as a temporal prediction system, improving the temporal precision of attentional fluctuations in sensory gain, that in turn control the sampling of sensory information. This mechanism is implemented through a top-down influence of low-frequency oscillations, originating from the motor cortex, onto ongoing excitability fluctuations in the sensory system via the dorsal stream. Overall, these results are compatible with Active Sensing theories, which emphasize the prominent role of motor activity in sensory processing, through its close interaction with attention.

P2-002

NEUROMAGNETIC AUDITORY STEADY STATE RESPONSE TO TRIADS: MODULATION AS A FUNCTION OF FREQUENCY RATIO

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Perceptual degree of consonance and dissonance of a chord varies as a function of frequency ratio between component tones comprised in the chord. Generation of a dissonant sensation in tonal system is known to be associated with the auditory steady-state response (ASSR) phase-locked to difference frequencies which are salient in chords with complex frequency ratios. However, no studies have taken into account the intrinsic neuronal characteristics of the ASSR, which reflect the acoustic properties of the sound signal such as carrier frequency (fc), modulation frequency (fm), sound pressure level or spectral energy of each frequency component. This study therefore investigated more precisely how the neuromagnetic ASSR would be systematically modulated as a specific function of frequency ratio (2:3:4, 4:5:6, up to 14:15:16), when the chords were characterized by identical spectral number (3 frequency components), equal energy (70 dB SPL) and same difference frequency (ΔF=fm at 41.6 Hz). The response characteristics to fc, varied between 128 and 624.51 Hz, were compensated by utilizing responses to a sinusoidally amplitude-modulated sweep tone ascending and descending through the corresponding frequency range. The results showed that the strength of the ASSR moment as well as phase-locking to fm was stronger for the chords with complex frequency ratio than for those with simple frequency ratios. Since the spectral and temporal characteristics of the sound envelop (fm) were identical among the chords, it is presumed that the regulatory pattern of the fine structure might be the key to understand the generation of consonance/dissonance sensation.

P2-003

THE EFFECTS OF PREDICTION AND ATTENTION ON GAMMA AND ALPHA OSCILLATIONS IN VISUAL CORTEX

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Attention and stimulus intensity both have effects on the oscillatory power of MEG signals in visual cortex. Directed attention suppresses contralateral alpha power in occipital areas, while attention directed to a stimulus enhances the power of the gamma oscillations it induces. Stimuli with higher contrast also induce greater gamma power. However, the oscillatory characteristics of backwards predictions have not been examined. Additionally, evidence from evoked responses does not provide a clear account of how attention and prediction interact.

Predictive coding accounts of brain function suggest that top-down predictions should enhance beta-band synchrony mediated by deep pyramidal

cell layers of cortex, while stimulus strength should enhance bottom-up connections conveyed by gamma synchrony originating from superficial pyramidal cells. Attention is hypothesised to act as a gain control, multiplicatively interacting with the effects of bottom-up stimulus strength and top-down prediction.

In this study we investigate the interactions between oscillatory power in prediction, attention and modulation of stimulus strength. Participants were presented with matrices of Gabor patches which rotated randomly for 1-2 seconds. A letter or scrambled letter composed of aligned Gabor patches (with high or low levels of jitter) emerged from background and were displayed for 500ms. Prediction and attention were manipulated with precues and post-stimulus probes. Participants were asked to identify the presence or absence of a letter in the stimuli. 306-channel MEG was recorded. We use standard Beamformer and time-frequency analysis to investigate the effects of changes in bottom-up stimulus strength, directed attention and top-down prediction on oscillatory power in alpha, beta and gamma frequency bands. We also examine how attention and prediction interact in the modulation of evoked gamma responses to stimuli. We discuss how these results relate to predictive coding accounts of brain function.

P2-004
INHIBITING IN THE FACE OF A SMILE OR A FROWN

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Social-cognitive functions provide a basis for our daily interactions with others. The ability to inhibit inappropriate behaviours is one such function, while emotional face processing is another. Inhibition is commonly tested using a Go-No go task; will including emotional faces in a Go-No-go protocol enable the two functions to be tested concurrently?

Twenty young adults (10 female) completed an emotional faces Go-No go task in the MEG (CTF 151), where angry and happy faces were presented rapidly with either a blue or purple frame; subjects responded as rapidly as possible to only one of the colours. Two conditions were run; one where 75% go trials established the prepotent response tendency, requiring inhibition on 25% of trials and the reverse where only 25% required responses, and inhibition was not invoked. Vector beamforming was used to localize brain activity associated with both inhibition and emotional face processing. Image contrasts were used to identify areas with significant condition differences in activation.

When inhibition was required, bilateral activation in the inferior frontal gyri (IFG) and insulae was found. A contrast between the emotional faces showed early increased activation to happy faces in the left IFG and lower activation for happy faces in the right superior temporal gyrus. Bilateral inferior parietal activations were identified in the inhibition condition when comparing the two emotions, with increased activation in the left for angry and increased activation in the right for happy faces.

These patterns of findings are consistent with the literature regarding Go-No go tasks, providing further evidence of the importance of IFG during inhibition. The use of emotional faces within an inhibition task produced additional insula activity, suggesting that a Go-No go task with emotional stimuli activates a wider network and could be valuable for assessing frontal-parietal as well as limbic involvement in clinical populations.

P2-005
AN MEG STUDY OF THE COCKTAIL-PARTY EFFECT USING THE COHERENCE FUNCTION BETWEEN A BRAIN SIGNAL AND A SOUND ENVELOPE

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Objective: In our previous study, we have demonstrated that the coherence function between a sound envelope to the ear of a subject and the MEG response of the subject is a useful tool to analyze “cocktail-party effect”, where we have used monaural sounds. An objective of this study is to investigate if stereo sounds from different directions give further knowledge or not.

Methods: We presented stereo mixture sounds to the subject by using a pair of ear tube from outside of the MSR and instructed to notice the sound that we mentioned beforehand. There were two kinds of mixture sounds, music and voice. In addition, we performed experiments with triple mixture sounds that sources are located at the left, center and right direction. The subject was right-handed, and showed contralateral dominance for the stimulated ear in AEF measurement using tone bursts. We used a 160-channel whole head MEG system developed by KIT and recorded MEG signals during the sound presentation for 3 min. After preprocessing (off-line filtering and down sampling), the coherence functions between sound envelopes and MEG signals were calculated.

Results: The noticed sound showed higher coherence values than the unnoticed sound, and they were distributed over the contralateral hemisphere for the sound source direction. In case of triple mixture sounds, there were three distribution patterns of the higher coherence values for the noticed sound. Those are left-hemisphere dominance for right sound, both-hemisphere dominance for center sound and right-hemisphere dominance for left sound. As difference between music and voice, the voice sound showed comparatively high conference values in the left hemisphere regardless of the sound source direction.

Conclusion: The results showed the subject extracts the sound by using the difference of the sound lateralization. Linguistic factors also seem to be used for the voice sound discrimination.

P2-006
GENERATION OF THE MISMATCH NEGATIVITY REQUIRES PERCEPTUAL AWARENESS OF THE STANDARD STREAM

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The mismatch negativity, or MMN, is one of the most-studied components of the auditory-evoked response. Elicited by any violation of an otherwise regular stimulus sequence, generation of the MMN has long been thought to be automatic and preattentive, even subconscious. By embedding classical auditory-oddball sequences in a multi-tone informational-masking stimulus, we show instead that generation of the MMN occurs only when listeners are perceptually aware of the standard stream prior to the occurrence of the MMN-eliciting deviant stimulus. Deviants occurring during unperceived standard streams failed to elicit an MMN despite clear representation of both standards and deviants in primary auditory cortex. The results strongly suggest that the MMN reflects violations of the regularity of conscious stimulus representations in non-primary auditory cortex.

P2-007
THE INDIVIDUAL ALPHA FREQUENCY DECREASES BY DOPAMINE IN PATIENTS WITH PARKINSON'S DISEASE.

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Next to the well known motor symptoms also cognitive functions are modulated by the depletion of dopamine in the cortico-striatal network in Patients with Parkinson's Disease (PD). To assess the neural underpinnings of these symptoms we examined the oscillatory activity during an attention task. We focused on the alpha band (7-13 Hz) since this frequency was found to be crucial for this task. The MEG (Elekta Neuromag oy., Vector View, 306) of 20 patients was measured while performing a visuo-spatial attention task. Once without dopamine replacement medication (OFF) and once after the administration of L-Dopa (ON). We scored the Unified Parkinson's Disease Rating Scale (UPDRS) before and after the administration of L-Dopa, to assess the severity of the disease symptoms and to assure the L-Dopa had an effect. The UPDRS-scores significantly improved from OFF to ON. To examine the effect of L-Dopa on alpha band activity we assessed the individual alpha frequency (IAF) of each patient during the OFF and ON session. This was done for four one-second time-windows in the same task: (1) Baseline, (2) Cue presentation and subsequent delay, (3) Delay and (4) Presentation of a bilateral visual stimulus. The results showed that the IAF significantly decreased after administration of L-dopa. More interestingly this effect was stronger during the baseline, cue and delay period then during the strong visual stimulation. Additionally, the IAF was strongly correlated with the UPDRS-scores, independently of medication state; the more severe the symptoms, the slower the IAF. Our results are in line with previous studies reporting a decline in cognitive performance after L-Dopa administration on specific tasks and other studies correlating a decrease in IAF with impaired cognitive performance. We propose that the decrease in IAF with L-dopa in PD-patients could reflect a general decline in cognitive functioning related to disease severity.

P2-008
A STUDY OF THE RELAXING EFFECT BY ANALYZING THE CONTINGENT MAGNETIC VARIATIONS IN MEG VIA THE STIMULUS OF AFFECTIVE PICTURES

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In this work we report the amplitude response of contingent magnetic variations (CMV) using MEG through the stimulus of affective pictures. We found that the CMV amplitude in unpleasant task is always higher than the CMV amplitude in pleasant task at the left motor area, the center supplementary brain area and the right prefrontal area which are related to cognition process and a significant difference with a p value much less than 0.05 after t-test was demonstrated. Analyzing the strength of Mean Global Field Power (MGFP) at alpha, beta and theta waves, we found that the MGFP amplitude of the alpha wave at center supplementary brain area, right prefrontal area, and left motor area is higher for subjects who receive unpleasant pictures than subjects who receive pleasant pictures. Additionally the mean value of MGFP shows $p < 0.05$ after the t-test. Only the MGFP amplitude at the beta wave (12-30 Hz) in the center supplementary area shows significantly statistical meaning with $p < 0.05$ after t-test. However, for the MGFP amplitude of the theta wave the data do not show significantly statistical difference after t-test in the center supplementary brain area, right prefrontal area, and left motor area. The data suggest that the MGFP amplitude of the alpha wave in center supplementary brain area, right prefrontal area, and left motor area is important for expressing relaxing state or stressed state. The MGFP amplitude of the beta wave is also an important parameter for indicating relaxing state or stressed state in the center supplementary brain area.

P2-009
EXPOSURE DURATION DIFFERENTIALLY AFFECTS PROCESSING OF EMOTIONAL AND NEUTRAL FACES

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Emotional face processing is a hallmark of social cognitive research. Neutral faces are less salient than emotional faces, and the degree to which the two are differentiated is widely used as an index of social competence. However, the effects of task parameters on relative salience between neutral

and emotional faces have not been thoroughly investigated. We addressed this question by using MEG to examine the effects of stimulus presentation duration on implicit processing of emotional and neutral faces.

Fourteen adults (5F, age 23.24 ± 1.96) were presented with a scrambled pattern and a face (happy, angry or neutral) on either side of a central fixation cross. Participants fixated on the cross, while indicating the location of the scrambled pattern with a button press. Each participant completed the task in two timing conditions (80ms and 150ms stimulus presentation duration) for a within-subjects comparison.

MEG data were co-registered to structural MRIs for all subjects, and eye movement artifacts controlled using ICA. Event-related beamforming analyses contrasting neutral and emotional faces showed that, 50-150ms after stimulus onset, both happy and angry faces elicited greater orbitofrontal activation than neutral faces within the 80ms condition, but not the 150ms condition, due to decreased activation to neutral faces only within the 80ms condition. Activation in left inferior frontal gyrus to neutral faces was significantly greater in the 150ms condition, equivalent to activity elicited by emotional faces in either timing condition.

These results show that, with longer stimulus presentation, neutral faces are able to garner attentional resources to the same degree as emotional faces, possibly due to more information becoming available. This suggests that even small changes in task parameters can impact effects of emotional salience.

P2-011
THETA OSCILLATIONS DURING COGNITIVE CONTROL: A COMBINED M/EEG STUDY

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Cognitive control refers to the management of executive functions. Theta oscillations are the most commonly studied signature for cognitive control, especially with EEG. Although previous EEG investigations have identified induced theta over mPFC during conflict, no study has looked at the brain sources that contribute to theta-oscillations that are associated with conflict. A simple paradigm to examine conflict is a Simon task, in which subjects respond according to stimulus color while ignoring task-irrelevant spatial information. We collected simultaneous EEG (56 surface electrodes) and MEG data (275-channel whole head biomagnetometer; MISL) during a Simon task. Time-frequency decompositions of mid-frontal EEG sensors (Cz) show an increase in theta oscillations around 400ms for incongruent vs congruent trials (conflict response) in all subjects. In the MEG sensor data, a similar contrast (between incongruent vs congruent trials) did not reveal such a consistent pattern. We reconstructed MEG sensor data across multiple frequency bands including the theta band, and found multiple sources spread bilaterally across prefrontal cortex that contribute to conflict. These data strongly indicates that a strong radial component source for theta oscillations is seen reliably in EEG, and multiple tangential sources across prefrontal cortex that are also active in theta band, all of which contributes to conflict. Therefore EEG and MEG measure complementary information about cognitive control networks.

P2-012
CORTICAL OSCILLATIONS IN INHIBITORY CONTROL: EVIDENCE FOR A DIFFERENTIAL ROLE OF GAMMA AND THETA BAND ACTIVITY IN PERFORMANCE MONITORING

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We present results of a study on the functional role of frontal theta and high-frequency gamma oscillations and their inter-relationship during two types of inhibitory control tasks: go/no-go and go/switch. Neuromagnetic brain activity was measured in twelve right-handed adults while viewing rapidly presented visual cues. Subjects were instructed to respond to all non-target cues with a button press ("go" response), and inhibit their response to a rare target cue by either withholding responses entirely ("no-go" response), or switching response fingers ("switch" response). Errors were defined as default "go" responses to either "no-go" or "switch" cues. A transient increase in theta activity in the right frontal cortex immediately following both "no-go" and "switch" cue presentation was associated with correct responses, providing evidence for a common role in response inhibition. Furthermore, both frontal theta activity and high frequency gamma oscillations in the contralateral motor cortex were greater following switch responses and errors compared with "go" responses. The medial frontal theta oscillations preceding errors were similar in both tasks, but were greater for switch errors. Conversely, the power of the motor gamma activity was greater during errors following "no-go" cues compared with errors following "switch" cues. We interpreted increased theta power during errors as reflecting higher task engagement, leading to increased error awareness in the go/switch task. Additionally, our findings support the hypothesis that motor cortex gamma oscillations reflect motor intentions at the level of the motor command (corollary discharge), which may be greater for unintended movements such as response withhold errors. These results indicate a relationship between frontal theta associated with cognitive control and sensorimotor gamma oscillatory signals. These may have differential roles in monitoring motor plans and outcome during inhibitory control tasks.

P2-013
AMPLITUDE DIFFERENCES PRESENT AT ANTERIOR PREFRONTAL CORTEX DURING RESPONSES TO A VISUOMOTOR TASK IN ADOLESCENTS WITH FETAL ALCOHOL SPECTRUM DISORDER (FASD): A MEG STUDY.

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Exposure to substantial amount of alcohol in utero is known to produce a range of morphological and functional outcomes in offspring, which are collectively

called Fetal Alcohol Spectrum Disorders (FASD). The developing nervous system is particularly vulnerable to the teratogenic effects of alcohol. It has been documented that children with FASD exhibit a broad range of cognitive disabilities including deficits in intellectual functioning, memory, language, visual construction, number sense, and social cognition. Recent developments in neuroimaging have allowed us to probe the neural mechanisms underlying these deficits. We utilized a visuomotor task to probe differences in brain dynamics in 12 adolescents (12-19 years of age) diagnosed with FASD and 17 adolescents, with no reported prenatal exposure. Data were recorded with a 306-channel magnetoencephalographic (MEG) array. The task employed 100 trains of 6 – 8 visually presented cues. Subjects were told to make a motor response with the right index finger to each cue. The visual stimuli were presented for 350 ms, and had interstimulus intervals of 750 ms. BrainStorm (Tadel et al. 2011) was used to extract spatio-temporal patterns of activation in and adjacent to the anterior prefrontal cortex. There was evidence for differential amplitude in both left and right anterior prefrontal cortex in response locked data. In the left anterior prefrontal cortex, there were statistically significant differences after the 4th cue response. In the right anterior prefrontal cortex, there were statistically significant differences after the 1st through 4th cue responses. These differences in amplitude may contribute to disruption in attentional faculties (both endogenous and exogenous attention), as well as other cognitive processes in FASD.

P2-014
NEURAL ENTRAINMENT TO THE BEAT: THE "MISSING PULSE" PHENOMENON

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Most humans have a near-automatic inclination to tap, clap or move to the beat of music. The capacity to extract a periodic beat from a highly complex musical segment is remarkable as it requires forming an abstract internal model of the temporal structure of the stimulus. It has been suggested that the internal model of a beat is formed through non-linear responses that induce neural entrainment of cortical oscillations to the beat frequency, and that this entrainment gives rise to the percept of a beat. Here we tested this "neural resonance theory" using MEG recordings as individuals listened to sequences of rhythmic stimuli. Participants listened to 30-second long sequences of complex syncopated drumbeats designed so that they contain no energy at the pulse frequency (2Hz), similar to those used in a previous study by Chapin et al. (2010). We analyzed the spectrum of the neural activity while listening and compared it to the spectrum of the stimuli. We found that the neural response in auditory cortex resonated at the beat frequency, despite the fact that it was absent from the stimulus itself. Moreover, the strength of this beat-response correlated with individuals' accuracy in tapping the beat of these stimuli, as tested in a follow-up session. These findings demonstrate that neural activity at the beat-frequency in auditory cortex is internally generated rather than stimulus-driven, supporting the neural resonance theory. Critically, our results suggest that the neural entrainment to the beat is a fundamental mechanism underlying musical behavior.

P2-015
OSCILLATORY DYNAMICS OF RESPONSE INHIBITION: IT IS HARD TO HOLD YOUR HORSES WHEN DRUNK

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The ability to inhibit prepotent responses is an essential aspect of cognitive control. It is associated with right-lateralized frontal activity and with theta band oscillations. Conversely, motor preparation and execution are characterized by a decrease in beta power. Cognitive control is impaired by alcohol intoxication resulting in disinhibited, impulsive behavior. To examine the spatiotemporal characteristics of alcohol's effects on the neural dynamics of response control, event-related power in theta and beta frequency bands were measured during a Go/No-Go task with right-hand Go responses. Healthy social drinkers served as their own controls by participating in both alcohol (0.6 g/kg ethanol for men, 0.55 g/kg women) and placebo conditions in a counterbalanced design. Wavelet transforms for theta (4-7 Hz) and beta (15-25 Hz) frequencies were applied to whole-head magnetoencephalography (MEG) data. Total source power was estimated along the cortical surface using an anatomically-constrained minimum norm inverse. Alcohol reduced response accuracy only on No-Go trials. Response execution (Go) increased theta power in the left lateral and medial motor cortices. Successful response inhibition (No-Go) elicited an event-related theta power increase in a right-lateralized network at ~300ms including the inferior frontal, supplementary motor, anterior cingulate, and middle temporal cortices. Alcohol reduced theta only to No-Go trials, correlating with error rates, in this right-lateralized network. A decrease in beta power was observed during response preparation in motor and perimotor areas. It was followed by a strong rebound in the ventral prefrontal cortex, consistent with its inhibitory role in tasks requiring response suppression. In contrast to theta, alcohol did not affect beta power. Taken together, these results support the critical role of the right-lateralized network in response inhibition, with complementary contributions by theta and beta oscillations. The selective vulnerability of top-down functions to alcohol intoxication may contribute to impaired self-control and the inability to stop drinking.

P2-016
THE SPATIO-TEMPORAL ARCHITECTURE OF THEORY OF MIND PROCESSING IN A FALSE BELIEF TASK

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Theory of Mind (ToM) refers to the ability to attribute and understand mental states of others. Despite the onset of its development in preschool years,

ToM evolves over childhood and adolescence and in adults there is still considerable variability in this social cognition ability. Brain regions implicated in ToM have been identified in fMRI, but there is little work on the timing of neural activity involved in ToM processing. Thus, using MEG we examined the spatiotemporal dynamics underlying neural processing of a false belief protocol, the gold standard measure of ToM. Twenty adults were studied; all MEG data (CTF 151 system) were co-registered to each participant's structural MRI (Siemens 3T). Source analyses using vector beamforming were conducted on the contrast between false and true belief and the source locations provided the basis of the temporal analyses completed. MEG source power time-course reconstructions were generated and analyzed to determine the temporal architecture of neural activations specific to false belief reasoning. We found frontal and parietal regions to activate during false belief processing, primarily in the right hemisphere. Between 100-200ms the right temporal parietal junction (TPJ), superior parietal and orbital frontal regions ware active. From 200-300ms activation continued in the right TPJ, as well as the right precuneus, insula and orbital frontal areas. Thus, some of the areas associated with ToM (such as the TPJ) were active in this task with adults, and we extend previous findings by demonstrating the very early involvement of the TPJ with frontal regions in ToM processing.

P2-017

NEUROMAGNETIC IMAGING OF THE THALAMOCORTICAL BINDING NETWORK

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Connectivity in sensory systems involves reciprocal thalamocortical and cortico-thalamic connections with the thalamus acting as a communication hub. Oscillatory loops within the thalamocortical projections are tuned in the 40-Hz range and provide the neural mechanism for sensory binding through synchronous coupling. We developed an experimental procedure for synchronizing thalamocortical 40-Hz oscillations through auditory stimulation with amplitude modulated sound and vibrotactile somatosensory stimulation and recorded gamma oscillations with MEG. Stimulus events, which occur concurrently to the gamma oscillation inducing stimuli, caused a reset of 40-Hz oscillations and initiated a rebound. We analyzed with high precision the time courses of amplitudes and phases of 40-Hz oscillations. A new experimental approach of using central masking allowed us to separate contributions of gamma oscillations from the non-specific core network, which represents the sensory information, and the specific matrix network, representing an abstract auditory and somatosensory object as the result of binding. The results provides insight in the neural network underlying the interface between sensation and conscious perception.

P2-018

EFFICIENT INTEGRATION OF SOMATOSENSORY CORTEX IN PRE-STIMULUS PERIODS PREDISPOSES CONSCIOUS TACTILE PERCEPTION

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Conventionally in cognitive neuroscience, neural activity in pre-stimulus periods has been treated as 'noise'. However, recent MEG / EEG studies mainly focusing on the visual modality have shown that oscillatory activity prior to e.g. a near threshold stimulus influences its 'perceptual fate'. More specifically, pre-stimulus alpha band power (~10Hz) in task-relevant sensory areas is negatively correlated with conscious perception. This supports the notion that alpha oscillations reflect an inhibitory state of the respective neural tissue. The gating-by-inhibition hypothesis (Jensen and Mazaheri, 2010) links this local process to functional network architectures by proposing that alpha power modulations 'gate' information flow in distributed neural networks. Our recently published framework proposes in particular that distinct prestimulus connectivity states are beneficial for conscious perception ('windows to consciousness'; Weisz et al., 2014).

In the present MEG study, we set out to scrutinize our framework in more detail in the somatosensory domain using a task different from our previous study. We hypothesized that conscious tactile perception is preceded firstly by decreased alpha band power in the somatosensory cortex and secondly by enhanced prestimulus network integration of this task relevant area. Participants were asked to perform a tactile detection paradigm with stimulation at their perceptual threshold. As hypothesized, we found a relative alpha band power decrease in the somatosensory cortex but also premotor and superior temporal gyrus contralateral to stimulation prior to conscious perception. Furthermore, specific graph theoretical measures -assessing network integration- of somatosensory regions were associated with tactile stimulus detection in the pre-stimulus period. In a follow-up analysis, we show that pre-stimulus (somatosensory) alpha power on source-level is significantly correlated with peri- and post-stimulus time courses in sensors above the contralateral somatosensory area and parietal regions. These findings confirm our framework implying fluctuating network states to predispose conscious perception, thereby constituting a tactile window to consciousness.

P2-019

DELAYED ACTIVATION OF MENTAL FLEXIBILITY-RELATED BRAIN REGIONS IN MILD TRAUMATIC BRAIN INJURY PATIENTS AS DETECTED WITH MAGNETOENCEPHALOGRAPHY

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Despite a lack of observable brain damage during routine neuroimaging, patients with mild traumatic brain injury (mTBI) report adverse neurocognitive symptoms. However, recent studies using advanced neuroimaging techniques have shown microstructural tissue changes and mild axonal injury. This subtle brain damage can lead to functional deficits. We propose that magnetoencephalography (MEG), a non-invasive functional neuroimaging method with high temporal and spatial resolution, has the potential to elucidate the neural mechanisms underlying mild cognitive impairments. We used a mental flexibility task in the MEG to examine the effect of mTBI on brain processing involved in this executive function task.

16 adult patients with mTBI, within 3 months of injury, and 16 matched controls completed the Intra-Extra Dimensional Set-Shifting task in the MEG. MEG data were submitted to synthetic aperture magnetometry beamforming analyses to identify the spatiotemporal progression of brain activation. Significant group differences in regional activation were identified and their activation time courses were submitted to statistical testing to assess latency differences in brain activation between groups.

There were no group differences in accuracy, but the mTBI group showed significant delays in reaction time ($p<0.05$). The control group showed a task-related progression of brain activations in the insulae, dorsolateral frontal and parietal areas, consistent with findings in the literature. The mTBI group showed activation of these regions, but in a disorganized sequence. Time courses of activation showed significant delays among mTBI participants, in right insula and left posterior parietal cortex: canonical areas involved in cognitive set-shifting.

The marked delays in the activation of core task-related neural areas found in mTBI patients demonstrate that MEG can detect subtle neural changes associated with cognitive dysfunction and may eventually be useful for capturing and tracking the onset and course of cognitive difficulties associated with mild TBI.

P2-020

MODULATIONS OF POWER AND CONNECTIVITY PATTERNS IN THE BETA BAND PREDICT CONSCIOUS PERCEPTION OF UPCOMING NEAR-THRESHOLD VISUAL STIMULI

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Electrophysiological research has shown that conscious perception of near threshold (NT) stimuli can be predicted by modulations of oscillatory activity in relevant sensory areas as well as specific networks states. In the current study, we presented visual NT stimuli at a slow rate, within the inter-trial interval range of 3-6 sec, omitting any further information about the on- and offset of trials. During this continuous appearing presentation, participants were asked to respond whenever they saw a stimulus. We measured magnetoencephalographic (MEG) data in 20 young subjects during the NT task. Our analysis focused on the spectral power in the prestimulus time window (starting around 1 second before the stimulus). Remarkably, trials containing hits as compared to misses showed increased beta band power (around 17Hz). The neural generators of this effect were localized (using a frequency domain beam-former) to parietal areas, with a maximum in precuneus, and superior frontal areas. Interestingly and contrary to previous studies, we found no alpha activity (8-14 Hz) differences in the prestimulus period. Connectivity analysis (imaginary coherence) in the beta band seeded in the precuneus showed reduced connectivity of that area to sensory areas (visual and auditory) before hits as compared to misses. An increase in connectivity was found to frontal areas (different to the power effect). The precuneus is a major cortical hub and has been previously implicated in the so-called default-mode network. This task negative network is dominant during introspective cognitive states. Our observed coupling pattern between sensory areas and precuneus may therefore reflect fluctuating states of internal and external orientation, the latter being associated with a decoupling.

P2-021

IMPROVED FINE-CALIBRATION OF TRIPLE-SENSOR MEG ARRAYS

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We studied the interference suppression performance of the Signal Space Separation (SSS) method after fine-calibration adjustment of Elekta Neuromag® triple-sensor arrays. Each triple-sensor unit combines a magnetometer with two perpendicular planar gradiometers. Small cross-talk between the channels is corrected prior to calibration adjustment and before SSS processing.

The fine-calibration method optimizes: (1) The normal unit vectors of the triple-sensor units and relative calibration coefficients of magnetometer channels. Each normal vector is rotated in turn in small steps to find the best match between measured and modelled magnetometer data. Modelled magnetometer signal amplitudes for the best-match orientations are used to determine the

relative adjustments of magnetometer calibration coefficients. (2) Imbalance coefficients of gradiometer channels. Thin-film gradiometers diminish homogeneous magnetic fields by a factor of 1000. The remaining signal – due to slight imbalance between the two pickup loops – is modelled by a point magnetometer whose normal either points in the direction of the gradiometer axis (1D imbalance model) or is allowed to rotate freely (3D imbalance model). Imbalance coefficients of the gradiometers are searched by minimising the difference between measured and modelled gradiometer data.

With the standard factory calibrations, the SSS method can suppress external interference by factors lower than 40. Optimization of the calibration parameters yielded 3-4 fold increase in the shielding factor. There were some variations in the 1D-imbalance model shielding factors, while the fine-calibration optimization yielded significant improvements with the 3D-imbalance model. The 3D-imbalance model can enhance the performance of the present sensor array by improving the SSS software shielding factor at least by 100% when the external interference signal amplitude is large enough to allow such a high shielding factor to be determined, i.e., the residual interference is still above the sensor noise level.

P2-022

AN OPTICAL POLARIMETER FOR DC AND AC SUSCEPTIBILITY MEASUREMENTS OF SUPERPARAMAGNETIC NANOPARTICLES

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We present a simple optical experiment for static (DC) and AC magnetic susceptibility measurements of superparamagnetic fluids and films. We demonstrate the technique by measuring the B(H) dependence in static fields, from which we deduce the harmonic response of the samples to AC field excitation. The predicted AC response is confirmed by AC susceptibility measurements using the same apparatus. The application of an external magnetic field orients the magnetization vector of superparamagnetic iron oxide nanoparticles (SPIONs) along the field. In granular solids this orientation is determined by Néel relaxation, while in colloidal suspensions both Néel and Brownian (rotational diffusion) relaxation contribute. The B(H) dependence of these superparamagnetic materials is described by a Langevin function, and the sample magnetization induces an optical anisotropy that can be detected by optical polarimetry both in DC and AC measurements.

In our experiments we use the Faraday rotation of linearly polarized light to measure of the samples' magnetization. A 780 nm diode laser beam traverses the sample exposed to either a static magnetic field H or an oscillatory field H(t) produced by a solenoid. The Faraday rotation angle $\theta \propto B \propto M$ is measured by a balanced polarimeter whose differential signal is demodulated by a lock-in amplifier referenced to odd harmonics of the modulation frequency.

We recorded M(H) curves for different types of SPION suspensions. The anharmonic response of the samples to AC excitation produces signals at odd harmonics of the drive frequency whose amplitudes are in agreement with predictions from the experimental M(H) dependences. At low excitation amplitudes the phase-sensitive detection of θ(t) permits measurements of the real and imaginary susceptibilities' frequency dependence. Particle size distributions are inferred from model fits of the χ'(w) and χ''(w) curves.

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P2-023

LOW-COST, HIGH PERFORMANCE INSTRUMENTATION FOR BIOMAGNETISM

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SQUID magnetometers have unparalleled magnetic field sensitivity, which has enabled substantial progress in the field of biomagnetism over the last several decades. The recent advance in atomic magnetometer (AM) technology, however, has raised the possibility of a new low-cost, user-friendly alternative to SQUID magnetometers. AMs have the potential to dramatically expand the use of biomagnetism for research and commercial applications. We present experimental results with our newly-developed compact AMs for biomedical use with sensitivity similar to that of SQUID magnetometers (5 fT/√Hz). These AMs operate at room temperature and can be manufactured at a small fraction of the cost of SQUID biomagnetometers. In head-to-head comparison in a clinical environment, we show that our AMs provide nearly identical data as SQUID magnetometers for Magnetocardiography and Magnetoencephalography applications. These results indicate that AMs will be ready for commercialization in the very near future.

P2-024

CALIBRATING THE NEW MEG SYSTEM IN NAPLES

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Accurate sensor calibration [1-3] is a preliminary procedure for the efficient use of a multichannel MEG system. The final goal of calibration is the estimation of the sensors parameters, i.e. their locations, the vectors orthogonal to the helmet surface and their sensitivities, whose actual values may differ from the nominal ones because of thermal stresses.

Here we describe a calibration scheme developed for the optimal use of a MEG system realized at the Italian ICIB-CNR and recently installed in Naples (Italy). This whole-head MEG system consists of a 154 magnetometer helmet shaped array plus three additional triplets used as reference to perform noise reduction on the recorded data.

The calibration device consists of a set of 31 coils placed on a sphere at points equivalent to the corners of a dodecahedron and its reciprocal

icosahedron. These coils are sequentially activated for 33 seconds with a sinusoidal current produced by a dedicated circuit. In this way the coils can be activated from remote so that the system conditions do not change during the operation.

The computational step of the calibration procedure determines the nominal values of sensors and coils and compares them with the experimental magnetic field. Then the estimation of the actual values of the sensor parameters are obtained through an optimization procedure, based on the Nelder-Mead algorithm [4], which maximizes the correlation coefficient between the two magnetic fields. This procedure has been validated with synthetic data mimicking a real scenario. The results obtained with different optimization procedure will be compared.

References:

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[4] J. A. Nelderet al. Computer Journal 1965

P2-025
ATOMIC MAGNETOMETERS FOR MAGNETOENCEPHALOGRAPHY: DESIGN, CONSTRUCTION, AND VALIDATION OF A 36-CHANNEL SYSTEM

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We are developing a complete, 36-channel system for magnetoencephalography (MEG) based on an array of optically pumped atomic magnetometers (AMs) as the magnetic field sensors. With our AMs, we have achieved magnetic field sensitivities of 10 fT/Hz1/2 over bandwidths greater than 100 Hz. Our sensor array will be composed of 9 sensor modules, and each module will have a 40 mm by 40 mm footprint on the head. Since the AMs operate at approximately 150 °C, the sensor modules will be air-cooled to maintain the outer surfaces at temperatures appropriate for skin contact. The sensing volumes of each module will be located less than 1 cm from the head. Each sensor module will contain 4 AM channels, with each channel simultaneously able to detect 2 vector components of the magnetic field. One fiber-optic cable carries laser light to each of the sensor modules; to achieve 4-channel detection, the lasers are split into 4 beams inside each module. The AM channels will be spaced by 18 mm (in a square configuration) inside each sensor module. For MEG measurements, our sensor array will operate inside a human-sized magnetic shield. Thus, the footprint of our instrument will be much smaller than for current MEG systems, which generally operate in magnetically shielded rooms.

P2-026
TOWARDS MULTICHANNEL HIGH-*Tc* MEG SYSTEMS

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MEG systems based on high-*Tc* SQUIDs can achieve significant savings in energy and operational cost, in particular by avoiding problems with the supply of helium. A single-channel MEG system based on high-*Tc* DC SQUIDs with graphoepitaxial Josephson junctions and a 16-mm multilayer flux transformer has achieved a magnetic field resolution of ~3 fT/rt(Hz) at 77 K. The smaller total source-to-sensor spacing offers potential to increase the signal-to-noise ratio for a high-*Tc* MEG system compared to contemporary commercial low-*Tc* systems. However, multichannel high-*Tc* MEG systems have not been realized yet because of a number of issues associated with the integration of such SQUIDs in the dense arrays of sensors that are required for MEG systems. These points will be addressed and solutions proposed.

The technology required for producing sufficiently low noise high-*Tc* SQUID magnetometers with graphoepitaxial Josephson junctions has been developed (see [1] and [2] and references therein). High oxygen pressure sputtering allows deposition of large homogeneous areas of high-quality stoichiometric epitaxial heterostructures of superconducting cuprates with a mirror-like surface and superior electron transport properties. Scaling to a higher production rate can be achieved by using larger single crystal MgO wafers, which are available in sizes of up to ~10 cm. A special original layout of a high-*Tc* SQUID and feedback coil were used to reduce crosstalk between adjacent sensors. Estimates and measurements of cross-talk for different sensor configurations were performed. Further issues, including encapsulation of the sensors, their dense and flexible arrangement, vibration-free cooling and minimization of the sensor-to-head distance will be discussed.

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P2-027
BENEFITS OF ON-SCALP MEG

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We characterize the performance of a class of next-generation On-Scalp Magnetoencephalography (OSMEG) systems, which feature sensors located only a few millimeters from the scalp. The close distance to the scalp not only improves the signal-to-noise ratio (SNR), it also enables the system to capture a significantly higher number of spatial magnetic field dimensions than it is possible with existing MEG systems. We demonstrate the benefits of OSMEG by comparing it with existing MEG systems and with electroencephalography (EEG) systems that use the same sensor arrangements. To characterize the dipole localization accuracy, we perform an extensive set of simulations using extended sources, as well as, single dipoles, with simulated dipole locations across the entire cortical surface. Minimum-norm (MNE) methods are among the most commonly used distributed source localization methods. For these methods, we characterize the performance in terms of point spread and cross talk of the associated linear inverse operator. Finally, we compute the information-theoretic channel capacity for each system, which allows us to quantify the amount information gained under realistic noise assumptions. The results show that OSMEG can provide a drastically higher performance in all cases. The difference to EEG is particularly striking. If we assume the same number of sensors at virtually the same locations in OSMEG and EEG, OSMEG is vastly superior, as it is not affected by the low conductivity of the skull, which fundamentally limits the spatial resolution that can be achieved by EEG. We are confident that new sensor technologies, such as, atomic magnetometers or quantum diamond, will make OSMEG possible in the forseeable future, enabling neurophysiological imaging with unprecedented spatio-temporal resolution.

P2-028
MEG DETECTION OF SOMATOSENSORY EVOKED RESPONSES AT 1 KHZ USING AN ULTRA-LOW-NOISE SQUID SYSTEM

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Simultaneous MEG and EEG detection of ultra-fast somatosensory evoked fields and potentials (SEFs/SEPs) with frequencies above 1 kHz are reported. Such high frequency components reflect human cortical population spike activity and were up to now only accessible using invasive electrode recordings or state-of-the-art low-noise EEG setups. Detailed information about the spatial and temporal characteristics of both, population spikes and low frequency post-synaptic potentials (traditionally investigated by MEG/EEG) is required for the understanding of neuronal processing. In order to record ultra-fast activity by MEG, we developed an ultra-low-noise single-channel SQUID system designed for ULF-MR applications and MEG. By the use of an in-house upgraded low-noise dewar utilizing a fabric-like superinsulation in combination with a large pick-up coil (wire wound first order axial gradiometer: baseline 120 mm, diameter 45 mm) and a direct readout concept with close to negligible preamplifier noise contribution we achieved a system noise of 0.50 $fT/\sqrt{Hz}$ in the white noise regime. Electrical stimulation of the median nerve at 1.5 x motor threshold was applied to 5 subjects and the measurements were carried out inside a two layer magnetically shielded room. The measured high frequency SEFs (superimposed on the N20m) were found at ~20 fT (peak-peak) in the sigma range (450-750 Hz) and at ~2 fT (peak-peak) in the kappa band (850-1250 Hz). Interestingly, we find for the N20m and sigma-burst component a pronounced waveform overlap between MEG and EEG whereas for the kappa-burst only a partial overlap is observed, the latter indicating contributions from different kappa-burst generators. We are currently designing a multi-channel SQUID system with similarly large pick up coil geometries and its use will enable reliable source reconstruction of the ultra-fast SEFs.

P2-029
TOWARD AN ELIMINATION OF PRE-POLARIZATION ELECTROMAGNET FOR SQUID-BASED NMR WITH DYNAMIC NUCLEAR POLARIZATION

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A strong pre-polarization field is an indispensable field in the low field nuclear magnetic resonance (LF-NMR) experiment, because the micro-Tesla static field cannot generate enough nuclear spin polarization. However, there are some challenges in producing the strong pre-polarization field, which is one of the critical subjects in LF-NMR. A dynamic nuclear polarization (DNP) enables us to measure the enhanced signal by saturation of

the electron spin. Therefore, we can measure the LF-NMR signal at a low pre-polarization field. The enhanced proton signal of water within the 2mM TEMPOL solution was obtained by the DNP method at 49 μT. The enhancement factor was higher than 100.

P2-030
ADVANCED HELIUM LIQUEFACTION AND RECYCLING FOR MEG SYSTEMS

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Uninterrupted liquid helium supply is crucial for the routine operations of MEG systems. The typical liquid helium consumption by MEG is within the range of 10 to 14 liters per day. Today, most MEG centers still rely on external deliveries of helium storage tanks, while the increase in demand for liquid helium worldwide has led to more frequent price jumps, supply shortages, and delivery glitches, causing higher cost and anxiety levels.

The Advanced Technology Liquefier (ATL) offers a timely solution for helium liquefaction and recycling from within the MEG laboratories. The liquefaction rate of ATL160 at ~ 16 liters per day under 1 psi pressure is a perfect match for the normal boil-off rate of different types of MEG systems. In the Direct Recovery (DR) configuration, the boil-off from MEG is directly channeled to the ATL via sealed recovery pipes, and liquefied 100%. The loss during liquid transfer from ATL back to MEG is around 10 liters per transfer, which can be augmented by feeding helium gas from a storage cylinder to the secondary input on the ATL, while the MEG boil-off is recovered via the primary input. This dual-input design completely frees MEG centers from ordering liquid helium. The overall recovery rate of the DR mode can reach 80%. Further, the transfer loss is recoverable using the Medium Pressure Recovery (MPR) system by compressing helium gas into a storage tank with up to 100 psi pressure, which is then emptied by the ATL within one day.

ATL is easy to operate by users with basic liquid helium transfer experience. The mobility and maneuverability of ATL160 also makes the liquid transfer very similar to using the 100 liter storage tanks. There have been 10 ATL installations worldwide for all major brands of MEG systems with satisfactory performance results.

P2-031
OPTICAL PUMPED MAGNETOMETERS FOR MCG OR MFI APPLICATION

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Optically Pumped Magnetometers (OPM) are nowadays sufficient sensitive to substitute Superconducting QUantum Interference Devices (SQUID) e.g. in magnetocardiogram- (MCG) investigations. SQUID´s require liquid helium (4.2K) as a cooling medium which has to be refill usually at least once a week. Since OPMs work at room temperature, they are much easier to handle and furthermore the running costs are significant cheaper in comparison with SQUID-based biomagnetic devices.

Magnetic Field Imaging (MFI) is introduced as the advanced record of the MCG. MFI is a new method of diagnosis primarily developed to be applied in cardiology. MFI records the magnetic fields of the electrical activity of the heart with extremely sensitive magnetic sensors and successively stores, analyses and visualizes them. Both, the acquisition and analysis software use an integrated data base and have been developed by the company BMDSys Production to provide results almost immediately.

A 57-OPM-channel system was designed and manufactured in cooperation with the University Hospital Jena, Germany. The 57 channels are covering the whole human adult chest. It has been used in a clinical MFI-System in an aluminum shielded room with a chosen bandwidth between 0.016 and 250 Hz.

We present the MFI-results of first measurements with this OPM-system replacing SQUID-magnetometers.

One goal of the ongoing studies is to improve the device. Another goal is their application in magnetocardiography (MCG) or Magnetic Field Imaging (MFI), respectively.

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P2-032
DETECTING MCG SIGNALS FROM A PHANTOM WITH A 4HE MAGNETOMETER

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Purpose: Zero-field 4He magnetometer is a promising device to detect biomagnetic signals. It reduces the distance between the skin and the sensor, since the miniaturized device works at room temperature, without using

cryogenic systems or heaters. In this study, the possibility of measuring MCG signal with a 4He magnetometer is demonstrated.

Methods: A pseudo-MCG signal was simulated using a phantom consisting in a simple coil. The signal, injected by a generator, has been obtained with the ecgsyn, from the Physionet Toolkit (McSharry, et al. 2003). The coil generates a magnetic field around 70pT at 7 cm from the sensor along the vertical axis with a typical QRS shape. Our system, placed inside a 5 layer-µ-metal magnetic shield, is based on a first-order gradiometer configuration, with two miniaturized magnetometers. Each sensor contains a 100mm3 cylindrical glass-blown cell filled with 4He. The first sensor, placed 7cm above the phantom, measures the pseudo-MCG signal and the residual magnetic field B0, whereas the second one, several 10cm away, records mainly B0. The pseudo-MCG signal of interest is extracted as the difference one.

Results: Sensitivity of the first-order gradiometer developed is 1pT/√Hz at 1Hz and below 400fT/√Hz between 10 and 300Hz. After applying notch and bandpass filters, the main components of the cardiac cycle (QRS complex, P and T waves) are clearly recorded, well resolved and exhibit a morphology similar to the simulated MCG signal.

Conclusion: The developed sensor will be quickly used to record MCG signals on monkeys. A clinical trial is submitted for MCG recordings in healthy subjects. Several improvements of the present gradiometer will be implemented to increase the sensitivity in order to make MEG recordings.

McSharry, P, et al "A Dynamical Model for Generating Synthetic Electrocardiogram Signals." (Biomedical Engineering) 50, no. 3, p289-294 (2003).

P2-033

CARDIAC OUTPUT ASSESSMENTS AT SKIN LEVEL USING BIOMAGNETIC BLOOD PRESSURE RECORDS

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Introduction: There are a lot of patients around the world that present heart problems, where a medical diagnostic frequently uses the cardiac output for a direct evaluation or complement the medical evaluation.

Objective: An alternative method for the estimation of cardiac output measured at the skin is presented.

Methodology: A recently patented medical device was used in this study, and was tested by measuring the cardiac output of 10 patients (40 measures in total). This technique has the advantage of avoiding the direct damage to vessels because it measures the variations of the magnetic field generated by a magnet fixed on the skin, just over the blood vessels. The above process is performed in order to convert the mechanical motions of the blood inside the vessels to an analogue signal and then, with a magnetometer at a fixed distance of 2.5 cm. The measurement is recorded and converted to a digital signal. Applying the formula CO = SVE * CF, the SVE is systolic volume ejection; CF is the heart rate, SVE is under normal conditions as long as, CF is the average value of signal.

Results: The cardiac output was obtained by measuring variations in the intensity of a magnetic field generated by the magnetic marker. Correlation parameters around $r = 0.9$ and $p < 0.05$ were found in this study using the new evaluation modality for the cardiac output vs. the thermodilution method.

Discussion: This is a procedure that gives information in a couple of minutes, so it could be an alternative for an express evaluation of cardiac output.

P2-034

HELIUM-FREE MEG RECORDINGS: SOURCE LOCALIZATION OF BRAIN ACTIVITY

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Today almost all MEG systems are comprised with low-*Tc* superconducting quantum interference device (SQUID) sensors to detect extremely small magnetic fields generated by the human brain. Although this technique is well established, construction and handling requires special materials and precautions. Moreover, low-*Tc* SQUID systems require cooling with liquid helium, which is quite expensive and resources are limited.

With this study we tested the feasibility of MEG signal acquisition and source localization utilizing a single high-*Tc* SQUID with a square 16 mm magnetometer input coil cooled with liquid nitrogen (77 K). In one subject neuromagnetic evoked responses generated by auditory stimulation have been recorded at 16 different positions above the left temporal lobe. In addition, resting state neuromagnetic fields were recorded for subsequent time frequency analysis. All experiments took place in a magnetically shielded room. The results obtained with the high-*Tc* SQUID system are compared to data from the same subject using a commercial 248 channel whole-head MEG system (Magnes 3600 WH, 4-D Neuroimaging) equipped with conventional low temperature SQUIDs operating at liquid helium temperature (4.2 K). The time-frequency representation revealed by the high-*Tc* SQUID system as well as the source localization of the auditory evoked field are in good agreement with results obtained using the commercial low-*Tc* MEG system. The neuromagnetic correlates of the evoked fields measured by both systems were localized in the region of the left primary auditory cortex. The deviation between the two current source estimates was found to be 7 mm.

Our results confirm that neuromagnetic source localization is indeed possible utilizing high-*Tc* SQUIDs. We believe that our findings will have implications in further brain research and developments of multi-channel high Tc SQUID based MEG systems.

P2-035
COMPUTING RESOLUTION FOR NEUROMAGNETIC IMAGING SYSTEMS

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Modern MEG systems are capable of whole-head coverage with simultaneous measurements of nearly 300 sensors. Such whole-head sensor arrays, together with advanced signal processing algorithms, now enable imaging of dynamic brain activity -- referred to as neuromagnetic source imaging. One problem with neuromagnetic imaging is that no established measure exists to assess the performances of imaging systems. At present, an index commonly used for assessing imaging system's general ability may be the number of sensors. Although one can imagine that a system with a larger number of sensors outperforms a system with smaller number of sensors, there is no method to quantitatively assess the performance improvements due to the increase in the number of sensors. On the other hand, the resolution has traditionally been used to assess the performance of wide variety of imaging systems. It is, however, difficult to define or compute the resolution for neuromagnetic imaging systems because the resolution changes depending on the locations and orientations of sources due to the space variant nature of the neuromagnetic imaging. This paper proposes a novel definition on the resolution, and develops a method to compute the resolution for neuromagnetic imaging systems. In this paper, using the resolution as a performance measure, various types of sensor hardware are assessed. Such assessments include performance improvements due to the increase in the number of sensors, and performance changes due to the change in the gradiometer baseline or change in the helmet size. This paper compares the performances between the planar and axial gradiometer systems and those between the conventional radial sensor system and a vector sensor system. We compare the resolution of two existing neuromagnetic sensor systems, MEGvision (Yokogawa Electric Corporation) and Elekta-Neuromag TRIUX (Elekta Corporate).

P2-036
MIXED SENSORS: SPIN ELECTRONICS-BASED MAGNETOMETERS FOR BIOMAGNETISM

WINNER 2014 JAMES ZIMMERMAN PRIZE

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Spin electronics have opened the field of numerous applications in data storage, magnetic field sensing or MRAM. In particular, spin valve devices offer very good sensitivity – below the nanotesla range at room temperature - but since these systems are field sensors and not flux sensors, their sensitivity is weakly dependent with their size, and they can maintain very good performance at extremely small scale, allowing integration of multiple sensors or very small size magnetometer.

Magnetometry addresses many fields, from industrial, as in car industry, to more fundamental problems like in space-magnetometry or biomagnetism.

Biomagnetism, being defined by the very weak signature of magnetic fields generated by living tissues and organisms, either by magnetic particles embedded or attached to cells, or by the electrical activity such as neural currents, requires extremely sensitive sensors to reach the picotesla to femtotesla range of the corresponding signals. Superconducting Quantum interference Devices (SQUIDS), operating at liquid helium temperature, have been the preferred type of sensors for this purpose.

We have developed a new type of magnetometer called mixed sensor, which combines a spin electronics field sensor with a superconducting pick-up loop, acting as a magnetic lens. This mixed sensor reaches field sensitivities in the femtotesla range in the thermal noise, and allows the recording of magnetocardiographic (MCG) signals. The principles of the mixed sensors and their operation for magnetic cardiac mapping will be shown in this contribution.

P2-037
LOW COST 3D MOTION TRACKING IN MEG

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Tracking motion during biomagnetic acquisition is a more and more interesting topic but technical solutions are relatively expensive and synchronization with MEG signals is not always solved. The main constraint for the tracking setup is to not perturb the measured biomagnetic field. Thus, tracking devices using moving metallic part are excluded. The tracking could be done using computer vision with shielded cameras or optic fibers bundle, but such devices are expensive.

We describe here how we performed low cost 3D motion tracking in Elekta Neuromag shielded room using only an existing video monitoring camera and a mirror.

To reconstruct 3D motion using computer vision, one needs at least two points of view. In our case, the first one is given by the video monitoring camera of the MEG-system, and the second one by a planar mirror positioned in the camera's field of view. Camera and mirror positions are tuned to have a good view of a colored target held by the subject. We did not notice major modifications of the biomagnetic signal induced by the immobile mirror.

We developed software which tracks the two colored objects - camera and mirror - in the movie of the experiment, and reconstructs the 3D trajectory of the target. We undertook a first precision measurement which gives an average error of 1cm.

To synchronise 3D motion with MEG data, a light is switched on at the time a trigger is sent to MEG electronics acquisition. The maximal time-delay of the synchronization is given by half of the refresh rate of the camera (1/50s in the present case).

P2-038

MAGNETIC RESONANCE IMAGING OF MOUSE HEAD IN ULTRA-LOW MAGNETIC FIELD

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We are developing a compact ultra-low-field magnetic resonance imaging (ULF-MRI) system which can be integrated with a magnetoencephalography (MEG) system for small animals based on SQUID techniques. This will be greatly beneficial to pharmacological and pathological studies that make use of small animals in experiments because it allows us to capture the biomagnetic signals and the anatomical images concurrently. In this study, we demonstrated the ULF-MRI measurement of a mouse head.

Our ULF-MRI system consists of five coil sets: a pair of circular coils for polarizing field and four sets of shielded planar coils for measurement field and 3D gradient fields. These coil sets were designed and fabricated at desktop size (350 x 350 x 188 mm3), in order to be installed inside a magnetically shielded box for small animal MEG systems. Especially, the four pairs of shielded planar coils were optimized by a target field method and homogeneities enough for ULF-MRI measurements have been obtained. A second-order low-*Tc* SQUID gradiometer and a multi-integrator type flux-locked loop circuit were employed to detect MR signals.

A mouse was anesthetized and laid at the center of the coil sets. The magnetic field strength at the measurement area was 33 μT; the corresponding Lamor frequency of protons was 1.4 kHz. The ULF-MRI measurement was performed by using the 3D Fourier imaging method to have the field of view of 40.8 mm and the resolution of 1.3 mm/pixel. The position of obtained MR image was in agreement with the region of the mouse brain.

P2-039

LOW TEMPERATURE SQUID SENSOR DEVELOPMENT – FROM SIS TO SNS

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Low Tc SQUID sensor development has made little progress, since its fabrication technology was established with inventing of the highly reproducible and nearly indestructible Nb-AlOx-Nb tunnel junction (M. Gurvitch, 1983). The Nb-AlOx-Nb sandwich generates superconducting-insulator-superconducting (SIS) junctions. On the other hand, superconducting- normal conducting-superconducting (SNS) junctions were studied in early days (J. Clarke, 1969), but could hardy find a place in the low Tc SQUID sensors, though many state-of-the art techniques like focused ion beam (FIB) milling and deposition have been applied to form them in sub-micron scales. In fact, products of the low Tc SQUID sensors are almost always the SIS type. The general requirements for a successful SNS junction technology to fabricate the SQUID sensors are the same as for the SIS junction: non-hysteretic I-V characteristics, high modulation voltage, reproducibility of junction fabrication, high stability under room temperature and thermal cycling, and low 1/f noise. Here, we present our challenge to make the low Tc SQUID sensor with the SNS junctions and our unique approach using the FIB to meet the above-mentioned requirements.

Figures of merit of the SNS type SQIUD sensor are as follows: First of all, it is not as fragile as the SIS type SQUID when being subjected to any unexpected current larger than 100 mA. Notice the SNS type junction has much higher current density than the SIS one. Second, thanks to its sub-micron-scale junctions, it has a relatively higher stability against magnetic fields, which opens the door for unshielded operation in the Earth's magnetic field and maybe even in low-field MRI environments. Third, it has less trouble with vortex trapping since the heater mounted in its printed circuit board has never been used. Based on the above figures of merit, we anticipate that the SNS type sensor will widen the fields and applications of SQUID in biomagnetism.

P2-040

INSTALLATION OF A HCS ON A MEG FOR CLINICAL USE

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We report the consequence of installation of a helium circulation system (HCS) on a magnetoencephalography (MEG) that is used for clinical use in a private hospital. The HCS re-liquefies all the evaporating helium gas using two 1.5 W GM cryocoolers, which was mounted on a commercialized MEG made by Yokokawa Electric Corporation Inc. in a private hospital. The developed HCS has an insert tube of the standard 0.5 inch diameter which enables easy installation on a working MEG in a short time without serious modification work.

P2-041

MEASURING DC IN THE HEAD IN A NEW WAY: USING THE PLANAR GRADIOMETERS IN A STANDARD ELEKTA MEG HELMET

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We have transformed the 204 planar gradiometer outputs of our Elekta MEG system so that DC (direct current) in the head can be directly seen online; the DC is seen as a map of arrows, looking down on the head. That is, we have performed an online inverse solution to approximately show DC. Because the gradiometers see only short range, we are insensitive to distant disturbances. We are therefore limited in sensitivity only by

internal gradiometer noise, about 0.4 pT/cm in a bandwidth of 0-4 Hz. For a measurement, the subject's head is first resting outside the helmet, and the arrows are reset. Then the subject puts his or her head in the dewar, and the new arrows are seen and recorded, perhaps in 3 seconds. Because we are detecting the gradients only, we lose the Bz which is uniform across the detecting coils; but this distribution of Bz can only be made by a distant source, of no interest, so we have lost nothing of value. Our method is useful because it is rapid, using only a single out-in motion. Looking at DC in the head with only one planar gradiometer was reported by one of us (Cohen) many years ago, where the only DC seen was due to pressing on healthy hair follicles. In our present effort, after about 15 sessions with a variety of subjects, we readily reproduce that follicle effect, but now simultaneously looking over the whole head, where the arrow pattern due to pressing is seen to be quite dipolar. Subjects with inactive hair follicles show other DC, probably also in the scalp, but with mechanisms and sources as yet unknown. We plan to address deeper DC sources, in the brain itself, after we better understand scalp sources, so they can be subtracted out.

P2-042

AUTOMATED MEASUREMENT OF THE ELECTRIC FIELD DISTRIBUTION INDUCED IN A SPHERICALLY SYMMETRIC CONDUCTOR BY TMS DEVICES

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Transcranial magnetic stimulation (TMS) is a non-invasive method for studying brain function. In TMS, a coil above the scalp is used to deliver a strong, brief magnetic field pulse that stimulates cortical neurons at the target site. The outcome of the stimulation depends, in addition to physiological parameters, on the intensity and waveform of the induced electric field (E-field). However, these factors are typically known only to a limited extent by the investigator. In fact, the stimulus intensity is often given simply as the percentage of maximum stimulator output (% MSO) although the effect of TMS is better described by the amplitude of the induced E-field. Furthermore, the stimulus waveform is commonly classified as either monophasic or biphasic, even though different coil dimensions and implementations in the stimulator circuits lead to variations in waveform.

We describe an automated measurement tool for mapping the E-field induced by TMS in a spherically symmetric conductor model of the head. We use our instrument to evaluate and compare E-fields of multiple commercial TMS coils and stimulator units. The measurement probe is based on the triangle construction, which was originally introduced for magnetoencephalography (MEG) and allowed saline-free implementation. Our instrument is able to automatically measure the E-field at any given point on a hemisphere.

The experimental results give us the calibration factors needed to convert %-MSO values to E-field amplitudes. Furthermore, they give us means to compare E-field maps and stimulus focalities of different coils. Such measurements help in ensuring that an investigator knows the properties of the applied E-field and that their TMS device works properly. Calibration of the stimulator output intensity may also make it easier to compare studies performed with different stimulators. In principle, the presented technology can be modified to be compatible with MEG calibration as well.

P2-043

MULTI-SENSOR TYPE ACTIVE MAGNETIC SHIELDING FOR UNIFORM AND LINEAR GRADIENT MAGNETIC FIELD COMPENSATION

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Biomagnetic measurement is sometimes disturbed by the environmental magnetic noises originating from the movement of trains or cars. A magnetically shielded room (MSR) with materials of high permeability is used to reduce such noise; however such shielding is very expensive, and the shielding factor in the low-frequency range is small. Thus, a variety of active magnetic shielding schemes have been developed to improve the shielding effect in the low-frequency range. Active magnetic shielding is a cheap and effective method for shielding magnetic noise that allows shielding the very low frequencies. In active magnetic shielding, it is possible to shield magnetic field sensor positions. However, there is a problem in which the shielding factor decreases at other positions. Also, the problem of cross-axial interference occurs when the magnetic field sensor cannot be installed at the center of the compensation coils, since the measurement object is installed at the center. In this study, an arrangement of the magnetic field sensors which solves these problems is proposed. This method installs pairs of magnetic field sensors symmetrically offset from the center along each axis. A total of six magnetic field sensors were used. The experimental demonstrations were carried out in two small models in order to prove the effectiveness of the proposed method. The result shows that a high shielding factor is obtained to a uniform magnetic field, even if the magnetic field sensor is not installed at the center. And large shielding area is obtained to a linear gradient magnetic field.

P2-044

MAPPING THE ELECTROMAGNETIC FIELD OF NEURONS AT CELLULAR SCALE USING ULTRA-SENSITIVE MAGNETOMETER

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We have developed a new generation of neuroscience tools to detect the electromagnetic signature of neurons at local scale. We use Giant Magneto-Resistive sensors (GMR) based on spin electronics, which offer the

possibility to be miniaturized and are sensitive enough to probe very small magnetic fields like those emitted by ionic currents flowing within neurons at cellular scale (in the picotesla to nanotesla range).

The probes developed called "magnetrodes" for magnetic electrodes are composed of two GMR sensors and an electrode allowing recording both magnetic and electric components at local scale. Some probes are planar, for recordings at mesoscale, and other probes with a needle shape are dedicated to microscopic scale. In this second type of probes, the sensors are located on a sharp tip allowing easy penetration in brain's tissues. The first magnetrodes fabricated reach a sensitivity of 3%/mT with a detectivity of 13nT/sqrt(Hz) at 30Hz and can detect signals from DC to a few kHz which allows recordings of Local Field Potentials as well as spikes. We will present the first experimental results obtained in-vitro.

P2-045

PRACTICAL CONSIDERATIONS FOR ACCURATELY RECORDING VISUAL STIMULUS ONSET TIMES WITH A PHOTODIODE-BASED CIRCUIT

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In a paradigm where participants are presented with visual stimuli, the precise time of their appearance on screen often needs to be recorded together with the MEG data in order to separate it into trials, for averaging across trials and subjects, and ultimately to compare results among studies. Because signals from the stimulus computer are usually delayed variably with respect to the actual display, timing is commonly recorded with a photodiode or phototransistor exposed to the projected images, and triggers (for immediate recording into trials) or markers (for later processing) generated when the measured brightness crosses a predefined threshold.

However, different factors influence the timing of these triggers: projectors display frames gradually from top to bottom, typically change light intensity relatively slowly and their overall brightness can decrease with time. Thus, one must define when the stimulus onset trigger should occur. The angular sensitivity and response speed of the light detector as well as ambient light may lead to missed or spurious triggers or cause jitter in time between trials and subjects as well as making it difficult to interpret the absolute times reported in works from different institutions.

In the described design, light from the projector is reflected and transmitted through an optical fiber cable to a phototransistor circuit. This avoids having metal and currents inside the magnetically shielded room. The circuit outputs an amplified version of the signal with low offset which can be used for precise post-processing, e.g. using software to detect and mark occurrences of light turning on and off. For immediate trial generation, a second copy of the signal is output, which has been filtered (high-pass) to reduce the rise time and remove any offset, allowing a threshold near zero, based on noise levels. Thus triggers can be generated reliably and as early as possible.

P2-046

DIRECT DETECTION OF LONG-LIVED NEURONAL ACTIVITY BY MEANS OF ULTRA-LOW-FIELD NUCLEAR MAGNETIC RESONANCE (ULF NMR) USING A PHASE ENCODING TECHNIQUE

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The usage of ULF NMR for direct neuronal current detection represents a promising attempt to improve the spatial resolution limit (~ 1 cm) of established methods like electroencephalography or magnetoencephalography. In the beginning we intend to detect emulated long-lived neuronal activity by performing in-vitro studies utilizing a head phantom with an integrated current dipole. According to the ULF NMR measurement principle, at first a strong magnetic field (~ 50 mT) generates a measurable magnetization within the aqueous solution of the phantom. Subsequently, a fast change to an orthogonally oriented detection field (~ 10 μT) induces a free precession decay (FPD). For its detection serves a first order gradiometer connected to a DC-SQUID current sensor. During the data acquisition, the long-lived activity acts as an additional local magnetic field that alters the FPD shape. However, we found that a cancellation effect prevents the detection of typical human current dipole moments (up to 50 nAm). In order to avoid this effect, the application of a spatial encoding technique in a direction perpendicular to the current dipole as well as to the detection field is needed. Space encoding was imitated by removing a part of the phantom volume below the current element. By this means the signal to noise ratio was not affected and current dipole moments as low as ~ 70 nAm could be detected. After integrating a one dimensional phase encoding into the measurement setup the resolution limit increased up to ~ 1 μAm. This decrease in sensitivity is attributed to image distortions resulting from the use of Fourier based reconstruction techniques in the presence of strong concomitant gradients. Thus, the application of correction algorithms and/or an adjustment of the measurement sequence should enhance the resolution limit.

P2-047

RAPID, DRY MULTICHANNEL ELECTROENCEPHALOGRAPHY

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Application of conventional silver/silver-chloride (Ag/AgCl) electrodes for electroencephalography (EEG) requires accurate, time-consuming individual preparation of each electrode position and application of additive electrolyte materials. These processes and materials increase patient stress, risk of skin irritation and limit acquisition time. Furthermore, they pose limitations

for mobility and measurement environment. Hence, conventional electrode caps are inappropriate for emerging EEG applications including brain computer interfaces, ambient assisted living and ubiquitous routine monitoring.

We present a novel, flexible dry-contact electrode technology for simple, rapid application and mobile EEG acquisition. Our electrode concept includes a flexible, compliant polymer substrate, subsequently coated with an electrically conducive layer. 97 dry electrodes were integrated into a flexible textile cap system providing reproducible positioning and adduction.

Based on a study on multiple volunteers, our results demonstrate the applicability of the novel electrode and cap system. For all volunteers more than 76 % of the electrodes provided impedances below 150 kOhm and sufficient signal quality for EEG acquisition. A further comparison to EEG signals, acquired using a conventional wet cap system, showed similar signal characteristics in time and frequency domain for an investigated frequency range between 1 and 40 Hz. The compared EEG episodes included spontaneous EEG, alpha activity and a visual evoked potential.

In summary, the electrode substrate and textile cap enable hair layer interfusion, adduction and adaptivity to the individual head geometry. The conductive coating ensures reliable and stable electrochemical characteristics as well as signal quality comparable to conventional electrodes. Thus, we conclude that our novel dry-contact electrodes can potentially replace conventional wet Ag/AgCl electrodes and allow for new fields of application of EEG acquisition and analysis.

P2-048

INTEGRATED OPTICAL MAGNETOMETER USING F=3 REPUMPER FOR SENSITIVE BIOMAGNETIC MEASUREMENTS

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Optical magnetometers integrated in anodically bonded silicon substrates provide identical working parameters in connected cells. This offers the possibility for complex magnetic field characterization as gradiometry or noise suppression. Especially, high lateral resolution of magnetic field sources becomes possible with either tightly arranged separate cells or larger cells with a high buffer gas pressure which are read out with photo detector arrays.

The price of high lateral resolution is the small active cell volume. This has to be counterbalanced by small relaxation rates of the atoms in the alkaline gas in the cells and/or a large signal. Both can be achieved with as many as possible atoms pumped into the same hyperfine and Zeeman levels.

To attain this goal, we use two lasers pumping integrated cells filled with cesium and nitrogen buffer gas. For measurement, the F=4 hyperfine level is pumped. The second laser repumps the F=3 level, resulting in a strong improvement of the magnetic field resolution. Detailed investigations of repumper configuration (D1 vs. D2 pumping, laser frequency and intensity) are given. As a result, with cells volumes of (4mm)3 a magnetic field resolution down to a few 10 fT/sqrt(Hz) is achieved in Earth's field strength.

Finally, some first attempts for biomagnetic field characterization are given.

P2-049

IMPROVEMENT OF SQUID MAGNETOSPINOGRAPHY SYSTEM TOWARD THE PRACTICAL USE IN HOSPITALS

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Objective: We are developing a SQUID magnetospinography (MSG) system. The MSG detects weak magnetic fields generated by the neural activity of the spinal cord using a SQUID sensor array. The neural current distribution around the spinal cord is reconstructed by the magnetic source analysis based on spatial filters. The functional information of the spinal cord is noninvasively obtained by the MSG and it helps accurate diagnosis of the spinal cord degenerative diseases. In this study, we improved the MSG system from the view of expanding the applications and saving running cost for the practical use in a hospital.

Method: The SQUID sensor array of the MSG system was upgraded to obtain the MSG signals from the area of 160 mm x 110 mm on the back of subjects in the supine position. The cryostat was also improved to reduce the frequency of liquid helium refilling. The improved MSG system was applied to the measurement of the cervical spinal cord evoked magnetic field (SCEF) from two normal subjects given repetitive stimulation to the left median nerves at their elbows.

Result: The cervical SCEF was successfully detected from both subjects with adequate signal-to-noise ratios. The anticlockwise rotation was observed in the transition pattern of the SCEF distribution. This transition pattern is typical for the cervical SCEF distribution induced by left median nerve stimulation. The transmission of the nerve signals along the spinal cord was also observed magnetically.

Conclusion: The improved MSG system had a sufficient performance for the SCEF measurement as well as the conventional prototype of the MSG system, even though the sensor array and cryostat were renewed.

P2-050

MAGNETOENCEPHALOGRAPHY BENCHMARKING EXPERIMENTS: HIGH- VS. LOW-*Tc* SQUIDS

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High critical-temperature superconducting quantum interference devices (high-*Tc* SQUIDs) can be potentially very effective for magnetoencephalography (MEG) signals because they allow a reduced sensor-to-scalp distance compared to low-*Tc* SQUIDs. Herein, we present results from benchmarking experiments in which a high-*Tc* SQUID and a low-*Tc* MEG system (Elekta Neuromag® TRIUX (Elekta Oy, Helsinki, Finland)) are compared in MEG recordings of auditory and somatosensory evoked fields (AEFs and SEFs, respectively) in humans.

While the high-*Tc* SQUID magnetometer can operate within ~1 mm of the subject's head [1], the typical sensor-to-scalp distance in the Elekta low-*Tc* system is ~20 mm. Via clinical-expert guided estimates, we know the typical scalp-to-source depths of neuronal sources are 15–20 mm for the SEF and 25–30 mm for the AEF. Considering the sensor-to-scalp distance, our high-*Tc* SQUID is expected to yield SEFs and AEFs with amplitude that are higher than that of the equivalent low-*Tc* SQUID by factors of 4–5.3 and 2.9–3.3, respectively.

Contrary to our expectations, but in accordance with previous results [2–4], the MEG signals were of comparable magnitude for the high- and low-*Tc* sensors.

To further explore the origin of the observed mismatch between the theoretical expectations and actual MEG recordings and to better characterize the current dipole source model at short sensor-to-source distances, we aim to perform further benchmarking on an MEG phantom (Elekta Oy, Helsinki, Finland) with 32 artificial current dipoles.

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P2-051
ASSESSING THE ADDED VALUE OF RECORDING MEG CLOSER TO THE CORTEX

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The sensitivity and spatial resolution of MEG are partly limited by the large distance between neural sources and the traditional low-*Tc*-SQUID-based MEG sensors. However, novel magnetic sensing technologies allow measurements at considerably shorter distances from the brain. Here, we conducted simulations in realistically-shaped geometries to quantify the performance of near-scalp atomic-magnetometer (AM) arrays using metrics based on forward models.

We compared the Elekta MEG system magnetometers (SQ) to hypothetical AM arrays, constructed by projecting the 102 sensor locations to 1 mm from the MRI-reconstructed scalp surfaces of 10 adults. We analyzed arrays that measure the normal component (nAM; 102 sensors) and tangential components (tAM; 204 sensors). We employed FreeSurfer to segment the cortical mantle from MRIs and distributed source dipoles along it. Source topographies for unit sources were computed using linear Galerkin BEM with three-shell models determined from individual MRIs. To compare sensitivities, we calculated the norms of the topographies and also studied the contributions of primary- and volume-current components separately. In addition, we quantified the similarities of topographies across sources and computed related spatial deviations and cortical areas.

On average across all cortical source locations, the sensitivities of nAM and tAM were 2.6 and 2.2 times higher than that of SQ, respectively. The primary-to-volume current ratios were 3.1, 1.0 and 2.6 for the nAM, tAM and SQ, respectively. For source locations with similar topographies, the spatial deviations were 13.3, 11.4 and 20.4 mm and the cortical areas 30.6, 21.7 and 75.7 cm2 for nAM, tAM and SQ, respectively.

Our simulations show that near-scalp measurements offer a clear performance advantage compared to current low-*Tc* SQUID-based sensing. The sensitivity increase and the availability of higher spatial frequencies should yield considerably more accurate source reconstructions.

P2-052
ON THE IMPORTANCE OF DIFFUSION MAGNETIC RESONANCE INFORMATION AS A REGULARIZATION TERM FOR MEG/EEG INVERSE PROBLEM

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Several regularization terms have been used to constraint the Magnetoencephalography (MEG) and the Electroencephalography (EEG) inverse problem. With imaging methods, regularization is needed because an accurate brain description requires a high dimensional space, but the solution itself is usually in a much lower dimensional space. It is known that cortex can be divided into several functionally homogeneous regions [1].

These regions can be identified using structural information coming from the diffusion Magnetic Resonance (dMRI) modality.

In this work, we investigate the importance of the dMRI information in the MEG/EEG inverse problem. Starting from the two parcel-based minimum norm inverse problem methods described in [2], we compare the source

intensities obtained by constraining the inverse problem by parcellations either obtained using dMRI parcellisation or with random clustering of the cortical nodes.

The stability of the solutions to the number of parcels and noise are also covered in this work.

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P2-053

QUANTITATIVE COMPARISON OF INTERICTAL AND ICTAL NEUROMAGNETIC ABNORMALITY IN CHILDREN ABSENCE EPILEPSY WITH MEG ACCUMULATED SOURCE IMAGING

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The objective of this study was to quantify the spatial and spectral differences of interictal and ictal brain activity from low- and very high-frequency ranges in childhood absence epilepsy (CAE).

Twelve patients with untreated clinically diagnosed CAE were studied with a 275-Channel whole head magnetoencephalography (MEG) system. MEG data were systematically analyzed in 9 frequency bands: delta (1-4Hz), theta (4-8Hz), alpha (8-12 Hz), beta (12-30 Hz), low-gamma (30-55), high-gamma (65-90 Hz), ripple (90-200 Hz), high-frequency oscillation(HFOs, 200-1000 Hz) and very high-frequency oscillations (vHFOs, 1000-2000 Hz). MEG sources were volumetrically localized with accumulated source imaging, a new method optimized for localizing spatial- and frequency-locked spontaneous brain activity.

In both low- and high-frequency bands, subjects with absence seizures showed different brain activities in the medial prefrontal cortex (MPFC), the precuneus (PC) and parieto-occipito-temporal junction (POT) between interictal and ictal states. Ictal MEG segments had higher odds of activities in the MPFC in the bands of 1-4Hz, 4-8Hz ($p<0.001$) and higher odds of activities in POT in the bands of 1-4Hz, 12-30Hz ($p<0.001$). Compared with interictal activities, ictal activities in the bands of 1-4Hz, 4-8Hz, 8-12Hz, 12-30Hz, 30-45Hz, 55-90Hz were increased ($p<0.001$).

Subjects with CAE during seizures are associated with increased MEG signals in both low- and high-frequency ranges as compared with interictal data. HFOs and vHFOs were detected by MEG with CAE patients both in interictal and ictal states. Accumulate source imaging strongly suggested that brain activities above 200 Hz are highly localized compared with low-frequency results. Noninvasive MEG approach with accumulated source imaging can be further optimized for detecting high-frequency brain activity.

P2-054

CHARACTERIZATION OF COGNITIVE IMPAIRMENTS IN SURVIVORS OF SEVERE SEPSIS BY MEANS OF MEG

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Beside functional disability, massive cognitive impairments are major determinants of long-term sequelae of sepsis. Diagnosis is difficult and so far long-term prognosis is not reliable.

In a magnetoencephalography (MEG) study we tried to identify cerebral impairments in survivors of severe sepsis and septic shock in the form of oscillatory steady-state responses to rhythmic visual stimuli to indirectly measure brain synchrony. The aim of this study is the identification of pathological oscillatory processing in sepsis survivors.

We recruited 25 survivors of severe sepsis or septic shock, who were investigated using magnetoencephalography (MEG). Cerebral oscillatory processing is seen as a significant parameter characterizing information processing in the brain. In this study, we analyzed resting activity and steady-state visual evoked fields (SSVEFs) in response to complex visual stimuli with familiar and unfamiliar objects. These objects were presented and analyzed at 7.5 Hz.

First results show that the rhythmic brain activity after visual flickering stimulation is altered in sepsis survivors in comparison to age matched healthy volunteers. We believe that the clinical manifestation of neurological deficits in terms of cognitive impairments results from pathologically synchronized neuronal oscillations and altered oscillatory coupling in the brain. Aberrant neuronal synchronization was already shown in another patient group, namely patients diagnosed with liver cirrhosis. The question arises whether the recent modifications found in survivors of severe sepsis are related to the damage of fibers connecting different brain regions or to a disturbance of the functional interaction between different brain regions or may be due to an atrophy of certain brain regions.

P2-055

EVIDENCE FOR AGE-RELATED EFFECTS IN AUDITORY ENTRAINMENT IN DYSLEXIA: AN MEG STUDY

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According to the Asymmetric Sampling in Time (AST) theory, hemispherical asymmetries in the neural structure of the auditory cortex make the left

hemisphere more sensitive to short timescales (25-50 ms: ~40 Hz) and the right to longer timescales (250 ms: ~4 Hz). Inappropriate sampling of the auditory signals could be responsible for the phonological difficulties of dyslexia. Previous studies reported both weak left hemisphere synchronization for fast oscillatory components of speech (in French) and weak right hemisphere synchronization for slow oscillations (in English). No study evaluated both low and high frequency synchronization in the same population. Thus, it is not clear if the observed effects are language dependent (a consequence of how language impacts on dyslexia) or not (inappropriate sampling cause dyslexia).

We focused on a different linguistic population (Spanish monolinguals with and without dyslexia) and evaluated how these effects change with age (studying both adults and children). Magnetoencephalographic activity was recorded whilst participant watched a silent movie and heard stimuli presenting amplitude modulated noise at low (2, 4, 7 Hz) and high frequencies (30, 60 Hz).

Dyslexic adults show weaker synchronization values and lateralization differences at 60 Hz and 30 Hz respectively. Dyslexic children (vs. control children) show atypical profiles due to stronger bilateral synchronization at high (30 Hz) and low frequencies (4 Hz) respectively.

Our results indicate that both children and adult dyslexics present differences at high frequencies compared to their corresponding matched groups, suggesting that synchronization effects are a consequence of how language impacts on dyslexia. Furthermore, in dyslexic children low frequency differences seem to play an important role too, indicating that the auditory synchronization phenomenon changes with age.

P2-056

IMPAIRED GAMMA-BAND RESPONSES TO AUDITORY WORD STIMULI IN AUTISM SPECTRUM DISORDERS

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Behavioral and neuroimaging studies have provided evidence of abnormal semantic processing in children with autism spectrum disorders (ASD). However, little is known about the neural basis of abnormalities in semantic processing of auditory words in children with ASD. In the present study, we hypothesized that children with ASD present impairments in semantic processing that could be reflected as reduced gamma-band responses while listening to words. To test our hypothesis, we studied three children with ASD (mean age 8y) and four age-matched (mean age 7.4y) typically developing (TD) children. The participants performed a lexical decision task where they listened to a randomized list of 420 words and pseudowords (presented 10% of the time) with an inter-stimulus interval of 1200-1500ms. Evoked fields were recorded during the experiment by using a partial coverage magnetoencephalography (MEG) system ("babySQUID", Okada et al., 2006) especially designed for pediatric use. The stimuli were presented to each ear separately via headphones. Participants were instructed to listen to the stimuli and respond by moving their index finger as soon as they heard a pseudoword. M100 auditory evoked response was identified in the ASD group peaking at ~99.3ms (14.15ms) for the left hemisphere (LH) and ~92.13ms (14.08ms) for the right hemisphere (RH). For the TD group, M100 peaked at ~91.85ms (11.34ms) for LH and ~80.85ms (5.50ms) for RH. Source localization was performed by using dSPM. M100 responses were localized in the primary auditory cortex for all children. Time frequency analysis showed decreased evoked activity in the gamma1 and gamma2 frequency bands for the ASD group compared to the TD group for both hemispheres. Our findings are in line with previous studies (Buard et al., 2013) and suggest an atypical modulation of high-frequency gamma oscillations in the processing of auditory words in children with ASD compared to TD.

P2-057

CHANGES IN PREFRONTAL ACTIVATION IN EARLY ALZHEIMER'S DISEASE: A MAGNETOENCEPHALOGRAPHY (MEG) STUDY

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It has been suggested that in early stages of Alzheimer's disease (AD), the brain may work harder to compensate for pathological effects; this is represented by activation of more cortical areas, and by concomitant slowing of overall processes. Such changes are also seen in normal ageing; in consequence, it is controversial whether neurocompensation is specific to AD and whether it can be consistently detected. Here, we conducted a pilot magnetoencephalography (MEG) study to investigate the so-called neurocompensatory response.

Fourteen subjects with early AD (age=75.7±5.8 years, education =14.9±4.2 years) and 16 healthy controls (HC; age=74.1±4.6 years, education=16.4±2.9 years) participated. Whole-head MEG scan (Elekta Neuromag Oy) was optimized to record both superficial and deep magnetic sources. Subjects were shown a series of graphical objects (50% had been shown prior to the test) and instructed to indicate whether the objects had been previously presented (i.e. "old") or not (i.e. "new"). MEG signals were synchronized to stimulus onset and time-averaged. Changes in activation for old>new and new>old were localized using event-related beamformer spatial filter to estimate a pseudo t-statistic, to perform the group mean activation maps ($p<0.05$).

With old>new, the right hippocampus/parahippocampal gyrus and the left inferior lateral frontal cortex were activated in HC, but not in AD groups. With new>old, activation in the right operculum, right insular, and the right inferior prefrontal cortices was seen in HC, but not in AD. Unilateral activation was

observed in HC in the occipital cortex (left) and the supramarginal gyrus (right); these regions were bilaterally activated in AD. In contrast to HC, the AD group showed increased activation in the right dorsal medial portion of the frontal pole.

Subjects with early AD did not involve certain key structures in episodic memory processing as seen in HC, but recruited additional neural circuits especially in the prefrontal cortex.

P2-058

COMPARISON OF MEG SOURCE ESTIMATION TECHNIQUES TO INTRACRANIAL EEG AND LONG TERM SEIZURE OUTCOME

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Background: Magnetoencephalography (MEG) source algorithm results are used to guide intracranial EEG (ICEEG) monitoring and determine areas for resection. The purpose of this study was to report our experience using equivalent current dipole (ECD) modeling/dipole scanning, current density reconstructions, and beamforming methods in a large cohort of pediatric patients with intractable epilepsy.

Methods: Source localization for each algorithm and seizure onset zone (SOZ), defined by ICEEG, were described by 3 reviewers according to 5 location criteria: (1) left/right (2) frontal/parietal/temporal/occipital/caudate/insula, (3) medial/lateral, (4) superior/middle/inferior (sub-lobar), (5) anterior/middle/posterior (sub-lobar). The accuracy of each algorithm was then compared to ICEEG. The relationships between the accuracy of these algorithms (discordant, lobar concordant, sub-lobar concordant) and long term seizure outcome was calculated using positive and negative predictive values (PPV, NPV).

Results: 32 patients were included in this retrospective review. No algorithms had sub-lobar concordance with ICEEG, including when algorithms were grouped by type (ECD modeling/dipole scanning, current density reconstruction, beamforming). Synthetic aperture magnetometry with excess kurtosis (SAM(g2)) tended to be the most accurate but there were no significant differences between algorithms. When comparing the source modeling with ICEEG findings, significantly more patients with a seizure free outcome were found to have lobar or sub-lobar concordance of ECD (66.7%), MUSIC (72.2%), MNE (58.8%), and SAM(g2)-VS (77.8%) (p = 0.02, 0.002, 0.009, 0.01). PPVs were highest for ECD (68.8%), and MUSIC (68.8%). NPVs were highest for SAM-VSsym (83%), ECD (71.4%), and MNE (68.4%).

Conclusions: This study describes the use of multiple MEG source estimation techniques and demonstrates that all algorithms have similar rates of concordance with ICEEG. Also, the concordance or discordance of ECD modeling/dipole scanning algorithms, such as ECD and MUSIC, with ICEEG were the best predictors of long term seizure outcome in a population of pediatric patients who underwent resective epilepsy surgery.

P2-059

SOURCE LOCALIZATION OF THE P300 EVENT-RELATED POTENTIAL AS A BIOMARKER FOR THE EFFICACY OF VAGUS NERVE STIMULATION IN PATIENTS WITH EPILEPSY

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Vagus nerve stimulation (VNS) is an adjunctive therapy for patients with refractory epilepsy. In VNS, a stimulator is implanted subclaviculary that can deliver electrical pulses to the vagus nerve. The working mechanism of VNS is currently unknown. This makes it impossible to predict whether a patient will benefit from VNS treatment or not before implantation. Therefore, we want to further investigate the working mechanism of VNS and find biomarkers that indicate the efficacy of VNS treatment.

In this study, the P300 component of the event-related potential during the auditory oddball task was investigated in VNS responders and non-responders under two conditions: VNS turned ON vs. OFF. The P300 component is modulated by the norepinephrine level in the brain, which has been linked to the anti-epileptic effect of VNS [1]. 60-channel EEG was recorded in 10 responders and 10 non-responders of VNS. The sources of the P300 wave were reconstructed using a template head model including scalp, skull, brain, and cerebrospinal fluid [2]. Multiple sparse priors were assumed as source priors for the inversion. Second level analysis was performed in the statistical parametric mapping software to find significant differences between the responder and non-responder group.

The statistical tests resulted in two findings. Comparing the ON condition with the OFF condition, we found a significant decrease in activity in the left inferior temporal gyrus in responders only (interaction group*condition p=0.015). A PET study also found this area to be significant [3]. For the OFF condition, comparing responders and non-responders, we found a bilateral decrease in activation in the inferior temporal gyrus (left:p=0.002,right:p=0.009). Although more research is needed, we showed the potential of EEG source reconstruction as a biomarker for the efficacy of VNS.

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P2-060

INVESTIGATION OF MOTOR-RELATED BRAIN ACTIVITIES IN PATIENT WITH WHITE MATTER DISEASE: A MEG STUDY

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White matter disease (WMD) is a dysmyelinating or demyelinating disease of the central nervous system of unknown etiology. The clinical usefulness of evoked potentials (fields) in diagnostics of the WMD has been examined. Somatosensory and motor evoked potentials (fields) are used to assess the integrity of sensory pathways. To provide quantitative data for improvement in motor activity by medication in WMD patient, we record motor evoked fields and compare the neuromagnetic data between pre and post-medication.

One female WMD patient with left weakness was studied. To investigate motor activity in the patient with WMD, motor evoked fields were recorded with a whole-head MEG system (KRISS, Korea) having 152 axial first-order gradiometers. During MEG measurements in pre/post-medication the patient was instructed to execute a cue-based tapping task (pushing button) by index finger on the affected and non-affected side, respectively. MEG waveform was segmented and averaged with a pre-stimulus baseline of 1.1 sec and a 0.3 sec post-stimulus epoch. We carried out equivalent current dipole method and time-frequency analysis to investigate effectiveness of the medication in the WMD patient.

In the results of behavioral test, movement performance of the affected side was significantly improved by medication (776.5ms to 327.5ms). The dipole of motor evoked response from the affected side was located in a well-focused motor area after medication (dipole strength is 12.6 nAm to 26.2 nAm and GOF is 84.7% to 91.9%). Delayed latency on the affected side recovered to the same level with healthy side (51ms to 26 ms). Readiness field in affected side was also appeared from -0.5 sec after medication.

In our results motor response after medication in WMD patient appeared in a well-focused motor area and quantitative data supported it. We conclude that MEG is one of useful methods to assess improvement of motor activity by medication in the WMD patient.

P2-061

MONITORING MOTOR-CORTEX PLASTICITY DURING STROKE RECOVERY USING PASSIVE MOVEMENTS

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Modulation of the 20-Hz rolandic rhythm to somatosensory input is believed to reflect alterations in motor cortex excitability. Using tactile stimulation, the strength of the rebound of this rhythm has been shown to be associated with the recovery of hand function. We followed (up to 1 month) the dynamics of the 20-Hz rhythm to both tactile stimulation and passive movement in stroke patients with upper limb paresis and in healthy controls.

Rhythmic brain activity was recorded in 22 patients (11 males, mean 69 years) at T0 (< 7 days after stroke) and at T1 (1 month after stroke) and in 22 healthy subjects (11 males, mean 59 years) with a 306-channel MEG system. Tactile stimuli were delivered to both index fingers alternately with an interstimulus interval of 1.5 s. For passive movements, the subjects' index fingers were extended (followed with flexion to the initial position) every 3 s. Temporal Spectral Evolution was utilized to quantify the modulation of the 20-Hz rhythm activity.

Passive movement elicited stronger rebound amplitudes than tactile stimulation both in control subjects and in the affected and unaffected hemispheres of the patients, both at T0 and T1 ($p < 0.05$). Importantly, in patients the rebound was significantly ($p < 0.05$) weaker at T0 than at T1 to both stimuli but it recovered to the level of the controls by T1. However, the suppression amplitude did not significantly differ between T0 and T1.

Passive movement is a stronger modulator of the 20-Hz motor cortex rhythm than tactile stimulation and therefore a more robust tool to study motor cortex alterations in stroke patients. Contrary to the suppression, the rebound showed changes during the early recovery process. Our results add to the evidence that plasticity occurs predominantly during the first month after stroke.

P2-062

DOPAMINERGIC MODULATION OF PATHOLOGICAL MOVEMENT-RELATED CORTICAL BETA RESPONSES IN PARKINSON'S DISEASE

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Parkinson's disease (PD) is a neurodegenerative disorder associated with motor, posture, and gait abnormalities. Human studies recording local field potentials within the subthalamic nucleus and scalp-based

electroencephalography have shown pathological beta synchronization throughout the cortical-basal ganglia motor network in PD. Suppression of such pathological beta has been associated with improved motor function, which may explain the effectiveness of deep-brain stimulation. Interestingly, dopaminergic medication has been shown to increase the amplitude of the pre-movement beta event-related desynchronization (ERD), but not the post-movement beta rebound (PMBR), in the subthalamic nucleus. However, it is unclear whether these treatment effects are present at the cortical level. In this study, we used magnetoencephalography (MEG) to investigate cortical oscillatory beta responses during right- and left-hand movement tasks in patients with PD, before and after administration of dopaminergic medication, and a group of healthy age-matched controls. Movement-related beta oscillatory responses were examined using beamforming to distinguish the brain areas and movement phases most affected by PD and modulated by dopaminergic medication. Unmedicated patients with PD exhibited significantly decreased pre-movement beta ERD compared to controls, as well as a marginal decrease in the PMBR during both right- and left-hand movements. Administration of dopaminergic medication increased the amplitude of oscillatory responses in both conditions and thus, had a normalizing effect. Neither oscillatory response amplitude nor laterality indices were affected by whether patients were moving their more or less affected hand, and dopamine therapy did not significantly modulate laterality indices. These data suggest that dopaminergic medications normalize movement-related cortical beta responses in patients with PD, but do not affect the laterality of the response. Additionally, these motor-related oscillatory responses are not affected by whether patients move their more- or less-affected hand. MEG studies may eventually help distinguish PD from disorders with overlapping symptomatology and be useful for tracking treatment responses.

P2-063
DEEP BRAIN STIMULATION MODIFIES MEG SIGNALS OF PATIENTS WITH PARKINSON'S DISEASE

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Intracerebral recordings have demonstrated increased beta-band activity in the motor networks of patients with Parkinson's disease (PD), and in animal models of PD. MEG studies have revealed less beta band activity in spontaneous cortical oscillations of PD patients than in controls. Treatment of PD with levodopa appears to enhance corticomotor coherence (CMC) in the beta band.

Deep brain electric stimulation (DBS) of subthalamic nucleus is an effective treatment of advanced PD. Its therapeutic mechanisms remain unknown. In animal models of PD the effects of DBS may be mediated via pathways connecting motor cortex and subthalamic nucleus. MEG recordings are well suited to study cortical oscillatory changes.

We recorded evoked fields and spontaneous MEG activity from PD patients treated with DBS. The stimulator-related artifacts were suppressed by the signal subspace separation with temporal extension (tSSS) method. With DBS on, auditory and somatosensory evoked fields are reliably detected from the tSSS-filtered data and are slightly enhanced compared with the DBS off condition. The spontaneous somatomotor activity in alpha and beta bands is not systematically modified by DBS. However, when DBS is on, their source strengths show significant positive correlation with PD rigidity. The CMC between somatomotor cortex and wrist extensors responds quite individually to DBS: both amplitude increases and decreases are observed when DBS is turned on. Low CMC peak amplitude in the beta band correlated with high rigidity and tremor scores when DBS was on in patients with good response to DBS.

MEG recordings during DBS reveal intricate changes in cortical oscillatory activity. The effects appear to be quite individual and do not explain the sometimes dramatic effects of DBS on clinical symptoms. The methodology is suited to study the effects of DBS on brain pathophysiology also in experimental therapies of e.g., epilepsy, depression, and chronic pain.

P2-064
CORTICAL OSCILLATORY CHANGES ASSOCIATED WITH HAND RECOVERY FOLLOWING CHILDHOOD STROKE.

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In childhood, good outcome from stroke is three times higher than in adults. We conducted an MEG study of changes in neural oscillatory activity in a group of children and adolescents recovering from cortical and subcortical strokes to better understand the mechanisms underlying this improved recovery rate. We predicted that enhanced motor cortical activity would be observed in patients with good outcomes, and would be more similar to the activity observed in controls, than in patients with poor outcomes. MEG data was recorded in seven patients (age 8 to 17 years, mean = 10.3 years) with both left and right hemisphere cortical and subcortical strokes and seven healthy controls while they performed a simple self-paced unilateral motor contraction task. Beamformer analysis of power changes in the beta band (15-35 Hz) was used to estimate the sources of movement-related cortical oscillations in contralateral and ipsilateral sensorimotor areas. Preliminary observations indicate differences between patients with good and poor outcome and between patients and healthy controls. In comparison to controls, in stroke patients the affected hand (and poorer outcome) was associated with multiple, weaker peaks of ipsilateral brain activity, and lower beta-band reactivity in the contralateral primary motor cortex. The motor cortex for the affected side also appeared to show increased high gamma activity range in patients with good outcome. Initial findings suggest that stroke patients with good and poor outcomes showed reduced beta-band reactivity compared to healthy controls, while those with good outcomes showed enhanced gamma activity which may reflect compensatory activation for the reduced beta reactivity and be a key factor supporting stroke recovery. Supported by the Stroke Imaging Laboratory for Children, the Ontario Brain Institute, and the SickKids Research Institute.

P2-065
A NOVEL METHOD FOR IMAGING TRANSIENT HFOS IN EPILEPSY MEG RECORDINGS

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The presence of high frequency oscillations (HFOs) in the range of 80 Hz and above in intracranial EEG is shown to be a marker of epileptogenicity and is associated with the ictal onset zone. Detection of HFOs in MEG recordings is more difficult because the signal-to-noise ratio (S/N) at high frequencies is generally poor. Transient HFO activity adds little to the total high-frequency power further reducing S/N when applied to long duration recordings. In order to contrast HFOs with normal background activity investigators have employed strategies such as comparing the power observed during ictal with that of interictal periods. However, the MEG recording may not include ictal activity. An unbiased algorithm for imaging HFO activity - not requiring visual parsing of a MEG epilepsy recording - has been developed. In the first step, an LCMV beamformer (SAM) is applied to the MEG data to estimate the source time series in the selected bandpass (e.g., 80-150 Hz). Next, a smoothed Hilbert envelope is computed from the source time series. Finally, the excess kurtosis is computed from the Hilbert envelope. A positive excess kurtosis indicates the presence of outliers (transient bursts) of activity within the selected bandpass. This process is repeated for all voxels within an ROI at the desired voxel spacing. Comparisons of interictal spike localization using SAM(g2) with that of HFOs (using the new algorithm) shows similarities but not identical spatial distributions.

P2-066
CORTICO-THALAMIC OSCILLATORY CONNECTIVITY IN PATIENTS WITH TREMOR

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Background: Deep brain stimulation (DBS) in the ventral intermediate nucleus region (VIMr), including the VIM proper and caudal Zona Incerta, is an effective treatment for patients with medication refractory tremor. Therapeutic effects of DBS are hypothesized to originate from modulation of cortico-subcortical network activity. However, little is known about the organisation of oscillatory network activity in cortico-thalamic circuits. To characterize the oscillatory cortico-thalamic network we performed simultaneous magnetencephalographic (MEG) and local field potential (LFP) recordings from the VIMr in 7 patients (age: 62 ± 2.8 years; 6m/1f) with parkinsonian (5/7) or essential tremor (2/7).

Methods: Simultaneous MEG-LFP recordings were conducted with the patients at rest with eyes open. LFPs were recorded bipolarly from adjacent contact pairs of the DBS electrodes. Dynamic imaging of coherent sources (DICS) beamforming was utilized to visualise peaks of frequency specific cortico-thalamic coherence in Montreal Neurological Institute (MNI) space. Significant clusters were identified using Statistical Parametric Mapping (SPM).

Results: Two spatially and spectrally distinct cortico-thalamic networks were identified. Prominent peaks of cortico-thalamic coherence were found in the contralateral temporal cortex for the alpha band (7-13 Hz), whereas significant beta band (12–35 Hz) coherence was focally distributed in the ipsilateral prefrontal cortex (Area 6, Area 44 Area 45).

Conclusions: Our results suggest a motor network characterized by beta band coherence between the VIMr and premotor cortex and the inferior frontal gyrus that is in line with previously reported cortico-subthalamic coupling studies in patients with Parkinson's disease. Alpha band coherence was predominant in the temporal cortex.

P2-067
COMBINED EEG/MEG CAN OUTPERFORM SINGLE MODALITY EEG OR MEG SOURCE RECONSTRUCTION IN PRESURGICAL EPILEPSY DIAGNOSIS

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Epileptic activity should be localized as close as possible to the spike onset to avoid propagation. However, the low signal-to-noise-ratio (SNR) limits the confidence in source reconstructions at these early time instants. In this study we investigated if combined EEG/MEG (EMEG) could increase the reliability in localizations compared to single modality EEG or MEG at early time instants. For this purpose a patient suffering from pharmaco-resistant focal epilepsy has been measured with simultaneous high density EEG (80 Electrodes), MEG (275 gradiometers) and afterwards with low density EEG (21 Electrodes) and stereo-EEG (sEEG 167 contacts). Following this, a high resolution six compartment finite element head model which comprises anisotropic white matter derived from diffusion-tensor-MRI has been constructed from individual MRI sequences. Furthermore, measured somatosensory evoked responses were used in an iterative fashion to calibrate patient specific skull conductivities following (Aydin et al., Plos One, 2014), which showed its importance for EMEG source analysis. The source reconstructions obtained with dipole scans showed that EMEG performs better than EEG or MEG alone at the spike onset. Source reconstructions at early time instants were closer to seizure onset zone and at the spike peak

they propagated to the pole of the temporal lobe. EEG and MEG source reconstructions alone were able to highlight just a subset of the spiking sEEG leads: anterior regions with EEG and posterior regions with MEG. EMEG results, on the other hand, were covering almost all relevant sEEG leads. Thus, we can state that using spike onset instead of peak could help avoiding mislocalizations due to propagation, and the complementarity of EEG and MEG enables a much more stable localization of these early and noisy signals in combined EEG/MEG scenarios.

P2-068

RESILIENCE OF OSCILLATORY BRAIN NETWORKS TO INTERICTAL EPILEPTIFORM DISCHARGES IS ASSOCIATED WITH COGNITIVE OUTCOME IN CHILDREN WITH FOCAL EPILEPSY

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Children with epilepsy experience abnormal neuronal discharges between seizures known as interictal epileptiform discharges (IEDs). IEDs may have a deleterious effect on the brain's intrinsic connectivity networks (ICNs) , which reflect the organization of functional networks at rest, and in turn on neurocognitive development. We investigated the effects of IEDs on ICNs in 26 children with focal epilepsy between the ages of 7 and 17 years using the spatial resolution of fMRI and the temporal resolution of MEG. fMRI resting-state data were collected and used to identify locations of brain regions comprising various ICNs using group ICA (FSL Melodic Toolbox). We then reconstructed broadband activity (1 – 150 Hz) for each source from resting-state MEG data over these spatial coordinates using a unit-noise-gain vector beamformer. The phase lag index (PLI) was then calculated between all pairs of sources for physiologically-relevant frequency bands. The graph theoretical measures, path length and mean clustering coefficient, were then used to characterize and quantify changes in network topology due to IEDs. We found that in both pre- and post-IEDs there were increases in network clustering, and decreases in network characteristic path length. Patients who were more resilient to these network topological changes had stronger ICN connectivity as measured by resting-state fMRI. Finally, we found that the children with larger network topological changes post-IED had lower IQ scores (R= -0.49, p=0.017). This study demonstrates that joint use of fMRI and MEG can be used to gain new insights into epilepsy. Additionally, due to the association between IEDs, ICN changes and neurocognitive outcome, these findings suggest there is clinical importance in suppressing IEDs to foster more typical brain network development in children with focal epilepsy.

P2-069

MULTIMODAL NEUROIMAGING EVIDENCE OF ALTERATIONS IN CORTICAL STRUCTURE AND FUNCTION IN THE AGING HIV BRAIN

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Combination antiretroviral therapy transformed HIV-infection from a terminal illness to a chronic manageable condition, but these patients remain at a significantly increased risk of developing neurocognitive disorders. Current evidence indicates that 35-70% of all HIV-infected patients exhibit at least subtle impairments on assessments of neuropsychological function. The pathophysiology underlying these impairments is not fully understood and previous functional MRI studies have been inconclusive. Some studies have reported hyperactivation in association areas of HIV-infected patients, whereas others found hypoactivation in sensory regions. In this study, we evaluate whether both patterns of abnormal neuronal activity coexist in HIV-infected patients, and whether these deficits reflect aberrations in brain structure, function, or both. Seventeen HIV-infected older adults and 17 individually-matched controls completed 3-Tesla structural MRI (sMRI) and a mechanoreception task during magnetoencephalography (MEG). MEG data was examined using beamforming methods, and sMRI data was analyzed using the latest voxel-based morphometry methods with DARTEL to generate maps of regional gray matter volume. We found significantly reduced theta responses in the postcentral gyrus and increased alpha activity in the prefrontal cortices of HIV-infected patients compared with controls. Patients also had reduced gray matter volume in the postcentral gyrus, parahippocampal gyrus, lingual gyri, and other brain regions. Importantly, reduced gray matter volume in the left postcentral gyrus was spatially-coincident with abnormal MEG responses in HIV-infected patients. Finally, left prefrontal and postcentral gyrus activity was correlated with neuropsychological performance and, when used in conjunction, these two MEG findings had a sensitivity and specificity of over 87.5% for HIV-associated cognitive impairment. This study is the first to demonstrate abnormally increased activity in association cortices with simultaneously decreased activity in sensory areas. These MEG findings had excellent sensitivity and specificity for HIV-associated cognitive impairment, and may hold promise as a potential disease marker.

P2-070

IDENTIFICATION OF INTERICTAL EPILEPTIFORM ACTIVITY WITH ICA AND AUTOMATIC COMPONENT IDENTIFICATION IN PATIENTS WITH NEGATIVE MEG RECORDINGS

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Introduction: MEG is a recognized tool for the localization of the interictal activities in epileptic patients. Unfortunately, there are patients that do not present abnormal activity during the EEG recording session to which localization procedures can be applied. We present here a method that combines independent component analysis (ICA) and lead field projection in order to reveal hidden abnormal activities.

Method: We used ICA in order to separate signals into independent time courses and their corresponding independent topographies. Although some components present an obvious origin, such as cardiac activity and eyes movement, some are more difficult to classify. We propose to select the components based on their compatibility with the lead field, i.e. how well they can be modeled as sources of cortical activity, in contrast with artifactual or non cephalic sources . This is done by a singular value decomposition of the gain matrix, followed by a projection of the components in the subspace that explain most of the gain matrix. After this spatial selection, a temporal selection is made either by visual inspection of the remaining traces or automatic detection of the abnormal (spike) activity.

Results and conclusion: This method is capable of revealing abnormal activities in patients presenting no visible epileptiform activity in the MEG signal after review by expert neurologists. These activities are pertinent in the context of corresponding depth recordings, obtained from the same patients. Our strategy enables the analysis of negative MEG exams as well as the automatic analysis of recordings with visible spikes.

P2-071

INCREASED VARIABILITY IN RESTING-STATE SENSORIMOTOR NETWORK ACTIVITY IN PAEDIATRIC BENIGN ROLANDIC EPILEPSY

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Benign Epilepsy with Centro-Temporal Spikes (BECTS) is a common childhood epilepsy characterised by sensorimotor seizures affecting mouth and face and high amplitude centrotemporal spikes. BECTS is associated with deficits in several neurocognitive domains including language and motor skills. Research in BECTS often focuses on the centrotemporal spikes, but these are not unique to BECTS. Here, we investigated background resting oscillatory activity in patients with BECTS and age-matched typically developing controls. We hypothesised that background activity would differ between patients and controls in the sensorimotor network but not elsewhere, and that differences would dominate in the beta band (13-30 Hz) due to its prominent role in network communication and motor processing. We used MEG independent component analysis to assess sensorimotor and visual resting state network activity by calculating areas of high temporal correlation in oscillatory activity across the brain. In the sensorimotor network, patients had a greater standard deviation of component amplitude than controls, suggesting greater (variability of) activity, whereas there was no difference in the visual network. Network values did not correlate with age. We also investigated activity in focal motor cortex by calculating variability of resting oscillatory time-frequency activity in unilateral M1 localised with a separate finger abduction task. The coefficient of variation in resting M1 peak frequency was greater for patients than controls in the beta band only, with a trend for a negative correlation with age in both groups. In addition, patients had a greater coefficient of variation in power for activity > 50 Hz. The latter may reflect High-Frequency Oscillations localised to seizure onset zone, or alternatively, a jaw or neck muscle artefact. Importantly, this high-frequency power variability is distinct from our findings in the beta band. The results may point towards a ‘disorganised’ functional sensorimotor network in BECTS.

P2-072

COMPARISON OF THE ELECTRIC FIELDS INDUCED IN THE BRAIN BY TRANSCRANIAL MAGNETIC STIMULATION USING FIGURE-OF-EIGHT AND DEEP HAC-COILS

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TMS is a technique for brain stimulation that is able to probe the brain circuitry and network in a non-invasive manner. In the past two decades, there has been a dramatic increase in the usage of TMS for studying the functional organization of the human brain as well as a therapeutic tool to improve psychiatric disease.

Standard TMS is applied with an electromagnetic coil called a round, or figure-of-eight (fo8) coil which is able to modulate superficial cortical regions. In order to reach deeper cortical or subcortical structures such as reward-related pathways directly, the stimulus amplitude for standard TMS coils needs to be increased. The use of standard TMS coils at such high stimulation intensities can lead to painful scalp stimulation. Furthermore, the risk of seizure is increased.

Deep transcranial magnetic stimulation (dTMS) is a modification of standard TMS, which was developed to enable effective stimulation of deep brain structures. The technology is based on a family of coil designs termed H-coils. The aim of the present study was to compare the field distribution of HAC-coil (one of the H-coils) and of a standard figure-of-eight coil. Three-dimensional electrical field distributions of HAC-coil designed for effective stimulation of deep brain regions such as the medial prefrontal and orbitofrontal cortexes, along with the anterior cingulate cortex and of a standard figure-8 coil were obtained in a realistic head model by employing impedance method. It was found that the fo8 coil induced fields focally under the coil’s central segment, at depths of up to 1.5-2 cm. While the HAC coil induced suprathreshold fields at depth of 4-6 cm from the scalp. The ability of the HAC-coil to stimulate effectively deeper neuronal structures is obtained at the cost of a wider electrical field distribution in the brain.

P2-073

ELEVATED LOW-FREQUENCY AMPLITUDE ENVELOPE CORRELATIONS DURING RESTING STATE IN MILD TRAUMATIC BRAIN INJURY

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Concussion, or mild Traumatic Brain Injury (mTBI), occurs when impact forces are exerted on the brain, and can result in a multitude of cognitive, emotional and perceptual symptoms. Diagnosis is currently difficult as there are few, if any, objective biomarkers using traditional structural imaging methods. In recent years, functional connectivity studies have shown that mTBI may be confirmed by atypical neural network interactions, such as changes in large-scale phase synchronisation and elevated spectral power. Recent evidence has also indicated that source-resolved correlations in band limited MEG power are relevant to the organization of functional brain networks at rest. Here, we used an MEG resting-state paradigm to investigate differences in functional connectivity between an mTBI group (n=20) and a healthy control (n=21) population. Participants fixated on a central 'X' for 5 minutes in relaxed wakefulness. Using an atlas-guided beamforming approach, 'virtual-sensor' time-series were extracted from 90 seed locations encompassing all cortical and sub-cortical regions in the AAL atlas. Amplitude envelope correlations were computed for all pairwise seed combinations at the delta, theta, alpha, beta, gamma and high gamma frequency bands. Results revealed that the mTBI group showed increased functional connectivity in the delta, theta, and alpha bands. Large-scale network differences were most prevalent in the theta band with the mTBI group showing increased connectivity between the right posterior cingulate cortex, sub-cortical regions (left putamen and globus pallidus), left temporal and medial orbitofrontal regions. Furthermore, metrics of connectivity between these atypical nodes correlated highly with measures of Inattentiveness in the mTBI group, a subscore from the Conner ADHD psychological assessment. These findings are consistent with previous literature showing mTBI patients display elevated low-frequency synchronisation, and we propose that these changes to neural synchrony may play a significant role in deficits of attention often seen following traumatic brain injury.

P2-074

ABNORMAL RESTING STATE FUNCTIONAL BRAIN NETWORK IN FOCAL CORTICAL DYSPLASIA

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Purpose: Despite of recent interest of network approaches derived from graph theory on epilepsy, resting state network analysis of focal cortical dysplasia (FCD) brain compared with control brain has not been adequately investigated. Here we investigated the difference in the resting state functional network between epilepsy patients with focal cortical dysplasia (FCD) and healthy subjects by using whole-brain magnetoencephalography.

Method: We retrospectively analyzed MEG signals from 35 epilepsy patients with FCD and 23 healthy controls. A global mutual information (MIglob) as a measure of strength of functional connectivity, and the global efficiency (Eglob) as a measure of efficiency of functional network were calculated for theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (31-45 Hz) bands to compare global network differences between FCD patients and controls groups.

Results: FCD brains at the resting state had stronger functional connectivity (MIglob) in the beta (p=0.000) and gamma bands (p=0.007), and also showed higher efficiency of functional network (Eglob) in the beta (p=0.001) and gamma bands (p=0.003) than controls. For the type of FCD, functional connectivity of FCD type I (MIglob, p=0.004; Eglob, p=0.012) and type II (p=0.016; Eglob, p=0.006) in the beta band were higher than that of normal controls. In the gamma band, the values of FCD type II were higher than those of normal controls (MIglob, p=0.001; Eglob, p=0.000) and FCD type I (MIglob, p=0.038; Eglob, p=0.031).

Conclusion: We revealed that FCD brains had increased functional connectivity in the beta and gamma bands at the resting state compared with those in healthy controls. Resting state network differences could be used even when there is no prominent interictal spike activity, and would enhance our understanding of epileptogenesis of FCD.

P2-075

EFFECT OF HIPPOCAMPAL SCLEROSIS ON FUNCTIONAL CORTICAL HUBS IN THE RESTING STATE

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Purpose: To test the hypothesis that mesial temporal lobe (mTLE) epilepsy patients with hippocampal sclerosis (HS) have different electrophysiological functional cortical hubs (highly central parts of the network) from that of healthy controls.

Methods: The resting-state functional networks in the theta, alpha, beta, and gamma frequency bands were evaluated in 44 mTLE patients with HS (22 left mTLE; age range 17~56, M:F=8:14; 22 right mTLE: age range 20~51, M:F =9:13) and 46 age- and gender-matched healthy controls. All patients achieved seizure-free after surgery. We investigated the network with betweenness centrality (BC) measures at the source level with magnetoencephalography (MEG) signals. A Kruskal-Wallis test and post-hoc Mann-Whitney test were performed to assess the group differences in BC.

Results: We showed the altered electrophysiological functional cortical hubs in mTLE patients with HS compared to healthy controls. Noticeably, the left hippocampus showed the significant differences among groups in the theta and alpha frequency bands. From a post-hoc analysis after correction for multiple comparisons, we found that the left mTLE patients showed the significant increase of the BC in the left hippocampus in the alpha band.

Conclusions: Considering that the node with high BC value can be regarded as a network hub of the network, our results suggest that the left hippocampus acts as a functional cortical hub in the left mTLE patients' brain. We presume that the removal of this network hub (a strong candidate of epileptogenic focus) led to the seizure-free outcome in the left mTLE patients with HS. Because there were no hippocampus related hubs in the right mTLE patients, clinical correlations should be considered. However, the resting-state analysis looking at the functional cortical hubs may help characterize mTLE, which ultimately may assist with diagnosis.

P2-076

WHAT GRAPH THEORY REALLY TELLS US ABOUT INTERICTAL MEG ACTIVITY OF FOCAL AND GENERALIZED EPILEPSY

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We analyze the complex network structure of resting state interictal magnetoencephalography (MEG) from two types of epileptic patients: frontal focal (FE) and idiopathic generalized (GE), and one of healthy subjects (HS), to elucidate whether epileptic brains behave differently to normal ones in the absence of epileptiform activity.

We studied 45 subjects: 15 FE, 15 GE and 15 HS. MEG data were recorded with a 306-channel Elekta Neuromag® system at 1kHz using tSSS with movement compensation. The analyses were performed on the 40 most stationary non-overlapping resting state segments of 5000ms per subject, far from recent epileptic discharges. We assess functional connectivity (FC) using a phase synchronization index termed Phase Locking Value (PLV) in the frequency bands: theta [4-8]Hz, alpha [8-12]Hz, beta1 [16-20]Hz, beta2 [28-32]Hz and low-gamma [44-48]Hz. Bivariate surrogates were used to test the significance of PLV between every two sensors. We characterize brain network structure by estimating a list of the most commonly used network measures. Then, we use the correlation between these measures to determine the minimum subset of them that fully describe the FC networks. Statistical differences between HS and the GE/FE groups were checked using a two-sided rank sum test.

Four sets of measures were single out: Global efficiency: differences reflect the facility of epileptic brains to "transmit information" or in the case of seizures straightforwardly propagate. Algebraic connectivity: suggests epileptic brains are more easily synchronized and have a more robust synchronized state than HS. Betweenness: was higher for HS in both beta bands, as was the eccentricity. This latter index was also higher in the FE group in the gamma-band

FC network measures detect an alteration of brain interictal activity in both FE and GE, indicating that in both types of epilepsy, the network of neocortical sources is more prone to become (pathologically) synchronized that in HS.

P2-077

REDUCED BETA BAND CONNECTIVITY DURING NUMBER ESTIMATION IN AUTISM

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Recent evidence suggests that disruption of integrative processes in sensation and perception may play a critical role in cognitive and behavioural atypicalities characteristic of ASD. In line with this, ASD is associated with altered structural and functional brain connectivity and atypical patterns of inter-regional communication which have been proposed to contribute to cognitive difficulties prevalent in this group. The present MEG study used atlas–guided source space analysis of phase synchronization in ASD participants, as well as matched typically developing controls, during a dot number estimation task which included stimuli with globally integrated forms (animal shapes) as well as randomly-shaped stimuli which lacked a coherent global pattern. Early task-dependent increases in inter-regional phase synchrony in theta, alpha and beta frequency bands were observed. Reduced long-range beta-band phase synchronization was found in participants with ASD at 70-145 ms during the processing of globally coherent dot patterns. This early reduction in task-dependent inter-regional connectivity encompassed numerous areas including occipital, parietal, temporal, and frontal lobe regions. These results provide the first evidence for inter-regional phase synchronization during numerosity estimation, as well as its alteration in ASD, and suggest that problems with communication among brain areas may contribute to difficulties with integrative processes relevant to extraction of meaningful 'Gestalt' features in this population.

P2-078

CORTICAL SOMATOSENSORY REORGANIZATION IN CHILDREN WITH SPASTIC CEREBRAL PALSY: A MULTIMODAL NEUROIMAGING STUDY

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Spastic cerebral palsy (SCP) is among the most common causes of physical disability in early childhood. It typically results from perinatal brain defects that alter the normal development of the somatosensory system. Here, we set out to characterize functional and anatomical abnormalities in the sensorimotor network associated with SCP with three different neuroimaging modalities. Ten children participated in the study: four children with diplegic cerebral palsy (DCP), three with hemiplegic cerebral palsy (HCP), and three typically developing (TD) children. Somatosensory evoked fields

were recorded with pediatric MEG in response to pneumatic stimuli to three fingers of both hands. Tractography analysis was performed on diffusion tension imaging (DTI) data for the fibers projecting from thalamus to the primary somatosensory (S1) and primary motor (M1) cortices. The sensory-motor resting state networks (RSNs) were examined using fMRI data. Tactile stimulation of the fingers elicited the first cortical response at ~50 ms in all TD and all DCP children, except in an HCP child having a large unilateral lesion. In 5 SCP children, the active regions showed abnormal somatotopic organization in the more affected hemisphere. In the less affected hemisphere and in the TD children, the active areas followed the normal somatotopic organization. Euclidian distances among S1 activities for the stimuli at different fingers were much larger for the HCP group for the affected hemisphere compared to the TD. Decreased fractional anisotropy and increased apparent diffusion coefficient were observed for the thalamocortical pathways in the more affected compared to the less affected hemisphere in SCP children. Rs-fMRI results indicated absent and/or abnormal sensorimotor RSNs for children with HCP and DCP consistent with the severity and location of their lesions. Our findings provide preliminary evidence of abnormal somatosensory processing and possible cortical reorganization in the sensorimotor network of children with SCP.

P2-079

GLIAL TUMOR LOCALIZATION AND CHARACTERIZATION USING DTI AUGMENTED MEG MODELLING

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Introduction: Electrical manifestations of glial tumors are observed at a macroscopic scale with clinical positive symptoms: epilepsy, sensitivity to anti-epileptic drugs and negative symptoms like functional losses and network related dysfunctions. Recent advances in molecular studies revealed neuron-like characteristics in glioma cellular populations. Available MEG and EEG studies in patients with glioma focus on wide scale time-frequency analyses and provide no direct insight in the tumor activity. Our purpose is to characterize the electrical interactions between the tumor and its environment.

Materials and methods: The study was approved by the regional ethics committee. We used MEG recordings during resting, passive and active tasks in 5 patients. A meta-model was computed using MRI T1 anatomical data and diffusion tensor imaging (DTI) connectivity data. The model is then parameterized using whole-brain MEG data and local derivations from the model are computed using Monte-Carlo methods. Model deviation magnitude is then projected on standard MRI images for visual assessment.

Results: In our preliminary results, model deviations were mainly observed inside the tumors and in the peritumoral space with long distance contralateral manifestations.

Conclusion: DTI enhanced MEG models are promising to localize and characterize brain glial tumors. We are planning quantitative analyses to establish a possible correlation between model perturbations and tumor grade.

P2-080

LOCALIZATION OF THE SPATIAL EXTENT OF THE GENERATORS OF EPILEPTIC DISCHARGES IN EEG AND MEG: COMPARISON BETWEEN 4-EXSO-MUSIC AND MEM APPROACHES

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Detection of spontaneous epileptic discharges in EEG/MEG from background brain activity requires synchronized neuronal activity over a minimum area of cortex to be detected from scalp recordings. A minimum area of 6-10cm2 has been suggested in EEG (Tao 2007) and of 4 cm2 in MEG (Oishi 2002). In the present study, we evaluated and compared the performances of two source localization methods dedicated to recover such spatial extent: 4-ExSo-MUSIC (Birot Neuroimage 2011) and the Maximum Entropy on the Mean (MEM, Chowdhury PlosOne 2013).

Both methods were evaluated using simulations of realistic epileptic discharges. We considered head geometry and sensor positions for a 275 gradiometers MEG device and for a 256-electrodes EEG system, obtained from the acquisition of a control subject. 10 realizations of three 10 cm2 sources configurations were simulated using a generative model combining realistic spatial description of the sources and physiological relevant models of temporal activities for both normal background over the whole cortex and for epileptic discharges along the simulated patch (Cosandier-Rimelé Neuroimage 2008). Detection accuracy of each method was quantified using area under Receiver Operating Characteristic (AUC) and spatial dispersion around the source (SD).

For both EEG and MEG, results showed AUC values greater than 0.8 in most conditions, suggesting that both methods are indeed sensitive to the spatial extent of the source. 4-ExSo-MUSIC showed slightly better AUC values, whereas MEM showed smaller SD distributions, suggesting that 4-ExSo-MUSIC might tend to slightly over-estimate the spatial extent, while MEM might tend to slightly underestimate it.

Whereas these preliminary results suggest excellent performance of both 4-ExSo-MUSIC and MEM when localizing spatially extended sources, more detailed simulations involving more than one generator and several extents will be investigated.

P2-081

WITHIN- AND CROSS-FREQUENCY ALPHA-BETA AMPLITUDE CORRELATIONS PREDICT REACTION TIMES DURING ACTION OBSERVATION

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When gearing up for action during attentive tracking of dynamic visual information, anticipatory neural activity is initially dominated by lateralized visual and extra-striate (BA39) alpha-band activity, and subsequently involves lateralized beta-band activity in visual-parietal and dorsal motor areas (Tan et al., 2013).

Yet, it remains unknown how these bilateral brain regions of interest (ROIs) are coordinated and modulated in their neural oscillations when processing dynamic sensory information for goal-directed response. Here, we further analyzed the neuromagnetic signals recorded while 12 participants attentively tracked an actor's pointing movement that ended at the location, which subsequently displayed the response-cue. Specifically, we assessed both within- and cross-frequency (alpha/beta) power correlations between these ROIs over time, and related these frequency-specific synchronies to response times (RT).

We observed a rich pattern of neural synchronies between visual-parietal and dorsal motor regions before response-cue onset that predicted RT. An increase in the majority of these within- and cross-frequency synchronies was associated with slower responses. Stronger neural synchronies yielding faster responses emerged in the minority of synchronies as a cascade of networks: An early alpha-alpha synchrony involving right BA39 with left visual (BA19) and primary motor (M1) areas, and beta-beta synchrony between left M1 and right premotor BA6. Subsequent alpha-beta synchrony between left BA18 and BA19, and alpha-alpha synchrony between left BA19 and premotor BA6 emerged before beta-beta synchronies involving left BA19 and BA18, left BA19 with bilateral BA6, right M1 and parietal BA7.

Remarkably, when a brain region engages with multiple other regions within the same time window, concurrent within- and cross-frequency synchronies are involved in coordinating the oscillatory brain patterns underlying anticipatory action. Notably, early sensory, higher cognitive, and movement brain areas can act as 'multiplexing' hubs and may do so with different temporal prominence.

P2-082

HOW STABLE ARE GAMMA OSCILLATIONS OVER TIME? SEARCHING FOR A GAMMA "FINGERPRINT" IN THE BRAIN

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It is well known that the human motor cortex exhibits transient bursts of high frequency gamma oscillations in the 60 to 90 Hz range during movement. Recent studies suggest that these gamma oscillations do not simply reflect sensory reafference, but have a facilitative role in motor control. In a previous study, we demonstrated that movement induced gamma bursts could be observed in MEG recordings during the performance of movements of different body parts (e.g., hand versus foot) and that these were highly similar in frequency and duration within individuals, and across hemispheres. This suggested that movement induced gamma oscillations in the motor cortex constitute a stereotyped spectral and temporal pattern or "fingerprint" specific to an individual and movement. To test this hypothesis further, we analyzed movement-related MEG data using a unique dataset from two right-handed subjects in which left and right self-paced index finger movements were repeated in separate sessions taken at the same time each day, over a five-day period, as well as at time points separated by several years. Time-frequency analysis of the beamformer derived source activity in primary motor cortex revealed highly replicable peak gamma frequencies in the same individual for the same movements, over repeated measures as well as over extended periods of time. This provides further evidence that an individual's motor cortex gamma is highly tuned to a preferred frequency for specific movements. We discuss our findings in light of recent evidence from developmental studies, which suggests that motor cortex gamma frequency may undergo larger changes early in life but become more stable during adulthood, potentially reflecting maturational changes in long-range connectivity in cortical and subcortical motor systems.

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P2-083

OSCILLATORY DYNAMICS REFLECT DIRECTIONAL UNCERTAINTY DURING MOTOR PLANNING

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Motor activity modulates oscillatory activity across multiple frequency bands. Here, we investigated the neurodynamics associated with the range of directional uncertainty during motor planning.

We recorded neuromagnetic signals while subjects performed an instructed-delay task. Ten healthy right-handed volunteers participated in the study. They used a joystick to control the position of a cursor. The task consisted of a 3 s center-hold period, followed by a 0.5 s cue and a variable 1-1.5 s memory period. The cue identified the region in which the upcoming target would appear. Three cue widths were used that provided 0 deg, 90 deg or 180 deg of directional uncertainty about the direction of the upcoming target. The target appeared at a random location within the region indicated by the visual cue. The subjects were instructed to move the cursor toward the target in a fairly straight manner.

As expected we found that the greater the range of directional uncertainty, the longer the reaction time. In addition we found transient increases in power in the delta and gamma bands linked to the onset of the visual cue and/or response. In contrast, the power in the alpha and beta bands showed a sustained decrease during the memory period of the task. Most importantly, only the sustained decrease of beta power was dependent on the size of the cue. The greater the range of directional uncertainty, the less

beta power decreased. The source of the change in beta power was localized in the precentral gyrus contralateral to the responding hand.

Although multiple bands contributed to the performance in the task, only beta power was associated with the level of directional uncertainty during motor planning. These results suggest that the power of the beta-band is an indicator of the level of motor preparation in the sensorimotor cortex.

P2-084
PREMOVEMENT POTENTIALS INDEX LEVELS OF PHYSICAL FITNESS

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Premovement neural activity reflects preparatory motor and cognitive processes associated with initiation of voluntary movement. The nature of this extended period of neural activity, believed to originate from supplementary motor and premotor areas, is poorly understood. Intensity of premovement neural activity is often related to cognitive factors such as vigilance, attention and cognitive load. Recent literature has suggested individuals with athletic backgrounds have faster reaction times and these advantages can be related to cognitive processing generated from known motor cortical areas. Reaction times in CNV tasks typically show larger amplitude premovement potentials with faster and less variable latencies. We hypothesized the ability to consistently and quickly respond under a low cognitive load task condition is related to physical fitness. Subjects with less active life-styles are thought to have restricted preparatory neural activity when undertaking motor tasks for extended periods of time. A "fixed" P300 paradigm (target appears every 5th stimulus) was utilized to assess reaction time and cortical premovement potentials recorded by magnetoencephalography (MEG). Four age-matched subjects performed a cued reaction time test for a period of 12 minutes. Equivalent current dipole (ECD) modeling is compared to virtual channel beamforming to assess premovement cortical activity correlated with reaction time. Individuals with a higher body mass index and less self-reported physical activity produced weaker movement-related cortical potentials and slower reaction times. Results are discussed in relation to the central governor model of exertion and fatigue during physical activity.

P2-085
MOTOR-CORTICAL OSCILLATIONS ASSOCIATED WITH SEQUENCE LEARNING

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Objectives: Motor learning occurs during practice but also between practice sessions. A specific significance of the primary motor cortex (M1) for early consolidation has been suggested. We here investigate alterations of motor-cortical oscillations associated with acquisition and early consolidation of a newly learned motor sequence.

Methods: Fifteen healthy subjects were trained on a serial reaction time task. Data were compared with performance during a randomly varying sequence. Event-related desynchronization (ERD) as a measure of cortical excitability at alpha (8-12 Hz) and beta (13-30 Hz) frequencies was investigated using a 306-channel whole-head magnetoencephalography (MEG) system. ERD was determined during initial motor learning and 10 minutes after skill acquisition (i.e. early consolidation period).

Results: The data revealed a stepwise decrease of ERD amplitude at beta frequency from random presentation to sequence learning and the early consolidation period. This decrease was significantly correlated with reaction times. As a main result the analysis revealed differences between implicit and explicit learning: Subjects using an explicit learning strategy in the early consolidation period showed stronger beta power suppression already during sequence learning than subjects keeping an implicit strategy.

Conclusion: The amount of beta power suppression during acquisition of a motor sequence may predict the switch from implicit to explicit learning during early consolidation.

P2-086
THE ROLE OF GAMMA CONNECTIVITY OF PREFRONTAL AREA DURING BEREITSCHAFTSPOTENTIAL

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Objects: Bereitschaftspotential (BP) is a slow negative cortical potential that is composed of early and late phase. The early and late component periods of BP are functionally different. Prefrontal cortex (PFC) is known as one of generators of early phase of BP and plays an important role in preparation for cognition and in decision making. In this study, we try to find out how the PFC gets involved in generating BP through the connectivity analysis.

Method: Electrocorticogram (ECOG) recorded from 4 patients with epilepsy. The subjects sequentially performed self- paced hand grasping for 5 minutes. Three sessions were recorded with each subject. Initially, common average reference (CAR) was carried out with the raw signal. Next, electrodes are selected which represented BP clearly by visual inspection, and an equal number of electrodes were chosen at non-PFC area as a

comparison model. We use a method the Partial Directed Coherence (PDC) as connectivity inference estimators between electrodes.

Results: In the PFC, Gamma connectivity of BP phase increased 24.39% on average during motor preparation or planning by comparison with the baseline for all subjects, whereas other areas excluding PFC decreased 31.36%. Also, it was found that the amount of connection between electrodes in PFC is much more than non-PFC during BP. These results were prominent in the early phase of BP, supporting previous studies that PFC is deeply involved in the early stage of BP generation.

Conclusion: We demonstrated that connectivity of gamma oscillation increased in the PFC compared with other regions, during BP generation. It implies that the PFC would contribute to generating the BP; in particular, the influence was maximized at the early phase of BP.

P2-087
IMPACT OF EXPERIMENT DURATION ON THE ACCURACY OF FUNCTIONAL MAPPING USING CORTICOKINEMATIC COHERENCE

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Introduction: Corticokinematic coherence (CKC) is a robust method for non-invasive functional mapping of the primary sensorimotor (SM1) cortex. This study investigates the effects of experiment duration on the accuracy of CKC functional localization.

Methods: Neuromagnetic signals were recorded with a whole-scalp MEG system (Elekta Oy, Helsinki, Finland) from ten right-handed healthy adults (3 females, mean age 31.1 years) performing continuous flexion–extensions of right-hand fingers at three different rates (~1Hz, duration 11min; ~2Hz, 5min; ~3Hz, 3min). Forefinger acceleration was monitored with a 3-axis accelerometer.

Coherence between MEG and accelerometer signals was computed using resampling method, i.e., 100 random selections of N epochs (N=25, 50, 100, 200; epoch length: 6144 ms at 1Hz; 3072 ms at 2Hz; 2048 ms at 3Hz). CKC sources were modeled at the peak amplitude of the cross-correlogram with equivalent current dipole (ECD). CKC accuracy was assessed by the radius of the smallest sphere containing 95% of the 100 ECDs modeled for each condition and subject. Sphere radiuses were compared using two-way repeated-measures ANOVA.

Results: In all subjects and conditions, ECDs clustered at the SM1 hand area contralateral to hand movements. Significant effect of movement rate and number of epochs was observed on CKC accuracy ($p<0.05$). From N = 25 to N = 200, the mean sphere radius decreased from 13.6mm to 4.7mm (1Hz), 11.8mm to 3.0mm (2Hz) and 11.0mm to 2.8mm (3Hz). Sphere radius lower than 5 mm required at least 100 epochs at 2 Hz and 3 Hz, and 200 at 1 Hz.

Conclusion: This study demonstrates a significant effect of movement rate and number of epochs used in coherence analysis on the CKC accuracy. Practically, reliable mapping is best achieved with fast movements, but might be achieved as well with slow movements at the expense of experiment duration.

P2-088
IMAGING SPATIAL REORGANIZATION OF FUNCTIONAL NETWORKS

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Introduction: Recent advances in our understanding of functional connectivity has revealed that network connectivity is non-stationary in time, spatially inhomogeneous and has spectral structure [1]. Here we present a methodology, based upon canonical correlation analysis (CCA), to task induced spatial reorganization of large scale distributed networks.

Methods: 10 right-handed participants were asked to execute a self-paced button press using the index finger of their non-dominant hand. MEG data were recorded throughout using a 275-channel CTF MEG system at a sampling rate of 1200 Hz. Data were filtered into the beta band (13-30 Hz) and reconstructed via Beamforming. The source time courses from the sensorimotor strips were extracted and analyzed using CCA across voxels. The resulting connectivity images (see [1]) were categorized into 6 groups using a k-means clustering algorithm and averaged

Results and Discussion: A set of spatially distinct modes of functional connectivity between the left and right motor strips were generated, each with an accompanying statistic showing the likelihood of the brain occupying a specific mode, a given point in time throughout the paradigm. One mode, with nodes in the left and right primary motor cortices (M1) showed a significant ($p_{corrected} < 0.05$) task induced increase in probability (0.81±0.12). This result validates the CCA method as a means to image spatial reorganization of networks, and is hoped this can be applied on more complex cognitive tasks.

[1] Brookes, et al. (2014) NeuroImage 91 282-299

P2-089
LATERALITY OF MOTOR IMAGERY BASED BRAIN ACTIVITY IS MODULATED BY REAL-TIME NEURO-FEEDBACK.

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Motor imagery (MI), the mental rehearsal of a physical task, is emerging as an effective treatment in neurorehabilitation, particularly stroke. MI effectiveness may be limited by the lack of feedback about performance. Neurofeedback (NFB) may overcome this limitation, as patients could see their brain activity

in real-time. This feedback may help improve MI performance, and provide the chance to modulate brain activity, a goal of neurorehabilitation. Prior to patient use it is critical to identify NFB as the factor driving brain changes during MI. Thus, this study examined the effectiveness of NFB during MI for 1) modulating brain activity; and 2) improving task performance.

Non-disabled participants assigned to a control (n=9) or NFB (n=9) group took part in 3 sessions of both actual and imagined performance of a seven-digit button press task. Neuroimaging was performed using magnetoencephalography. During MI, the NFB group received real-time NFB based on activity in the left and right sensorimotor cortex (SMC) derived from source level event-related synchronization/desynchronization (ERS/ERD) analysis in the beta band. Behavioural performance was recorded as the number of correct sequences during actual task performance pre- and post-MI.

Over time, the NFB group showed increased ERD in the SMC contralateral to the hand 'performing' the task during MI (i.e., lateralized brain activity). The control group did not follow this trend. Actual task performance improved significantly across sessions for all participants, with a trend towards better performance in the NFB group.

The provision of real-time NFB over multiple sessions leads to alterations in the laterality of brain activity. Further, results suggest that NFB during MI leads to a trend of improvements in actual performance of the imagined task. These findings have the potential to improve the effectiveness of MI as a neurorehabilitation intervention in patient populations.

P2-090

LOCAL COMPUTATION GLOBAL IMPACT: BRAIN OSCILLATIONS MAINTAINING THE SEGREGATION/INTEGRATION BALANCE AND OPTIMIZING BEHAVIORAL PERFORMANCE

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Characteristic local power fluctuations of sensorimotor alpha (~10 Hz) and beta (~20 Hz) oscillations are a robust finding in tasks in which spatial orienting of attention is manipulated. Fluctuations in oscillatory power are considered critical for task performance and behavior and are indicative for allocation of computational resources by means of segregation of task-irrelevant brain areas. Yet, little is known about the global impact of this locally observed changes on the brain's segregation/integration balance. Using MEG, functional brain connectivity via graph theoretical metrics served to test the hypothesis that "segregated" brain areas exhibit local power increases associated with globally distributed decoupling within the network and vice versa. Present results confirm previous findings of contralateral alpha power decrease and ipsilateral power increase associated with response planning and preparation in a delayed forced choice response task. A marked relationship between power and brain connectivity confirmed that alpha power decreases are associated with stronger coupling of task-relevant brain areas, while power increases reduce coupling to task-irrelevant brain regions. Furthermore, these connectivity patterns were mainly dominated by long range interactions and were associated with faster behavioral performance. Present results provide support for the active role of alpha/beta oscillations in shaping the brain's functional network architecture, thus optimizing behavior.

P2-091

LEARNING TO IMAGINE: BRAIN ACTIVITY FROM MOTOR IMAGERY PARALLELS THAT OF MOTOR EXECUTION AFTER REPEATED SESSIONS

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Motor imagery (MI) is a form of practice in which an individual mentally rehearses a motor task, facilitating skill acquisition in the absence of physical practice (Jeannerod, 1995). MI has many clinical applications, including brain-computer interface and stroke rehabilitation. While MI is thought to recruit similar brain regions as motor execution (ME; Hetu, 2013), this activation is influenced by differences in one's ability to perform MI (Wei, 2010). Therefore, MI may be considered a skill that must first be learned to efficiently facilitate skill acquisition. In showing that similar patterns of activation between MI and ME occur after repeated sessions of MI training, the current study demonstrates that the ability to use MI as a modality for skill acquisition is in itself a learned skill. Non-disabled participants (N=8; aged 18-35) performed both ME and MI of a unilateral seven-sequence button press task over three days. Magnetoencephalography (MEG) was utilized to capture neural activity, while rigorously controlling for muscle activity in MI blocks. Whole head dual-state beamformer analysis identified source-level ERS/ERD in the beta band (15-30 Hz; Schoffelen, 2009). 3D t-tests were used to compare activation patterns from Session 1 and 3 following Talairach normalization (Moses, 2010). Preliminary results indicate that while patterns of activation overlapped between MI and ME in Session 1, spatial extent was greater in the motor cortex during MI and additional areas associated with motor planning and preparation were recruited compared to ME. MI activation patterns more closely resembled ME in Session 3, with a reduction in both spatial extent of activation and number of areas recruited. These findings indicate that patterns of activity during MI become more similar to patterns of activity during ME after training. Thus, the current research provides direct electrophysiological evidence that the ability to perform MI is an acquired skill.

P2-092

DOES THE EFFECT OF TMS COIL ORIENTATION ON MOTOR EVOKED POTENTIALS DEPEND ON ELECTROMYOGRAPHY ELECTRODES ARRANGEMENT?

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Previous studies have shown that amplitude of a motor evoked potential (MEP) on hand muscles depends on coil orientation during transcranial magnetic stimulation (TMS). Nonetheless, this property might be affected by the system of electrodes used to record surface electromyography (sEMG) signals, e.g. placement and size of acquisition electrodes. Our hypothesis is that the effect of TMS coil orientation on MEP amplitude depends on the type of sEMG electrodes arrangement. In this study, we assessed the effect of TMS coil orientation on MEP spatial distribution and peak-to-peak amplitude with different sEMG configurations. MEPs were detected with a grid of electrodes (13 lines and 5 columns) over the abductor pollicis brevis muscle (APB) at eight different TMS coil orientations with respect to the midsagital line. Three distinct sEMG electrodes arrangements were adopted to compare the amplitude of MEPs: first, amplitude was calculated from the mean MEP detected by one group of electrodes in the grid, simulating the typical monopolar derivation. Second, amplitude was calculated from the MEP detected by a bipolar configuration simulated from two groups of electrodes in the grid. Third, the mean amplitude was extracted from the MEPs detected by the grid electrodes located over an active region of APB. In all cases the maximum MEP amplitudes were observed at coil orientations of 45° and 90°, in agreement with previous results. Maps of amplitude spatial distribution of MEPs showed a localized muscle activity at the distal portion of the APB muscle for all the coil orientations. Due to the relative small size and fusiform organization of hand muscle fibres, MEP amplitude at different TMS coil orientations did not depend on type of electrode arrangements. The localised activation of APB shows that this observation might not be reproducible for larger and compartmentalized muscles.

P2-093

ACUTE EFFECTS OF ALCOHOL ON RESTING-STATE ACTIVITY AND TASK-INDUCED GAMMA OSCILLATIONS IN HUMAN PRIMARY VISUAL AND MOTOR CORTICES

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Alcohol is a rich drug affecting both the γ-amino butyric acid (GABA) and glutamatergic neurotransmitter systems (amongst others). Recent findings from both modelling and pharmacological manipulation have indicated a link between GABAergic activity and oscillations measured in the gamma frequency range (30-80Hz). In this single-blinded, placebo-controlled crossover study, 16 participants completed two study days, one in which they consumed a dose of 0.8g/kg alcohol, and the other a placebo. MEG recordings of brain activity were taken before and after beverage consumption. During scanning participants viewed a visual grating stimulus for the first task, abducted their finger on hearing a tone for the second task and then completed 5 minutes of eyes-open wakeful rest. The paradigms used in both tasks are known to induce gamma-band activity in the visual and motor cortices respectively. For stimulus-induced responses, time-frequency analyses of beamformer source reconstructions in the visual cortex showed that alcohol increased peak gamma amplitude and decreased peak frequency. For the motor task alcohol increased gamma amplitude in the motor cortex. Cluster randomisation analysis of sensor-space resting-state MEG data revealed a significant power increase over central parietal areas in alpha (8-13Hz), beta (13-30Hz) and low gamma (30-50Hz) frequency bands. Acute effects of alcohol on resting state network connectivity were also investigated. These data support the notion that gamma oscillations are dependent, in part, on the balance between excitation and inhibition. Disruption of this balance by alcohol, by increasing GABAergic inhibition at GABAA receptors and decreasing glutamatergic excitation at N-methyl-D-aspartic acid receptors, alters both the amplitude and frequency of gamma oscillations. Increases in both beta and gamma power by alcohol during rest have not previously been reported at this dose or sample size. The findings provide further insight into the neuropharmacological action of alcohol.

P2-094

NEURAL DYNAMICS OF PREHENSION

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In everyday life, we continuously interact with people and objects within our social and physical environment. The most powerful and versatile tools we adopt within these complex interactions are our hands. Prehension, the capability to reach and grasp objects, is a clear example of the capacity of our hands to manipulate our environment. Even if this ability appears effortless and simple, the whole-brain network dynamics underlying its sophisticated control are still largely unknown.

We used magnetoencephalography to record brain activity from 20 subjects performing non-visually guided object-directed actions (grasping, reaching) using either the left or the right hand. An experimental trial comprised a planning phase, where the subject received instructions regarding the movement type and the effector, and an execution phase, where the subject had to perform the planned action.

We observed spectral modulations induced by the experimental conditions in different frequency bands (alpha, beta) within the fronto-parietal network involved in prehension coding. Our results highlight the role of beta band oscillations during hand action planning. A simultaneous increase (grasp coding) and decrease of power (effector coding) within specific regions of the

prehension network seem to allow the coding of specific actions performed with a specific effector. These different spectral changes seem to support the view of beta band modulations reflecting the summation of different processes rather than a unitary phenomenon consistent with results previously observed using other methods. This overview of whole-brain spectral modulations contributes towards a better understanding of the dynamics within the prehension system during the planning and execution of actions.

P2-095
THE REPRESENTATION OF OBSERVED ACTIONS – AN MEG ADAPTATION STUDY

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Observing other people's actions recruits similar frontal regions that are also recruited when we execute actions. It has been argued that the recruitment of frontal regions during action observation reflects the process of simulation, thereby providing access to the meaning of the action. Alternatively, frontal regions might be recruited as the consequence of action understanding, with the cognitive processes underlying action understanding being represented elsewhere, outside the motor system.

Here we asked where in the brain and at which point in time we can distinguish between different observed actions. To this aim, we used magnetoencephalography (MEG) in combination with a repetition suppression paradigm. Trials consisted of two subsequent videos (S1, S2) displaying simple center-out hand movements (pointing, grasping). We predicted that areas that are sensitive to the type of movement act should show stronger adaptation in trials in which S1 and S2 show the same movement („repeat" trials) in comparison to trials when the movement differs between S1 and S2 („non-repeat" trials). We computed time-frequency analyses and calculated differences between S1 and S2, separately for repeat and non-repeat trials. We observed a significant effect of adaptation for repeated versus non-repeated movement, as evidenced by a reduction of beta power being weaker during S2 in repeat in comparison to non-repeat trials. This adaptation effect was most prominent at left posterior sensors after 600 ms following stimulus onset. Our results provide new insights into the representation and the dynamics of observed actions, highlighting the importance of posterior, presumably visual areas.

P2-096
MOVEMENT-RELATED HIGH GAMMA OSCILLATIONS CAN BE ELICITED WITHOUT MOVEMENT BY MIRROR VISUAL FEEDBACK

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We tested whether mirror visual feedback (MVF) from a moving hand induced high gamma oscillations (HGO) response in the hemisphere contralateral to the mirror and ipsilateral to the self-paced movement. MEG was recorded in 14 subjects under three conditions: bilateral synchronous movements of both index fingers (BILATERAL), movements of the right hand index finger while observing the immobile left index finger (NOMIRROR), and movements of the right hand index finger while observing its mirror reflection (MIRROR). The right hemispheric spatiospectral regions of interests (ROI) in the sensor space, sensitive to bilateral movements, were found by statistical comparison of the BILATERAL spectral responses to baseline. For these ROIs, the post-movement HGO responses were compared between the MIRROR and NOMIRROR conditions. We found that MVF from the moving hand, similarly to the real movements of the opposite hand, induced HGO (55–85 Hz) in the sensorimotor cortex. This MVF effect was frequency-specific and did not spread to oscillations in other frequency bands. This is the first study demonstrating movement-related HGO induced by MVF from the moving hand in the absence of proprioceptive feedback signaling. Our findings support the hypothesis that MVF can trigger the feedback-based control processes specifically associated with perception of one's own movements.

P2-097
SIMULATIONS OF SPONTANEOUS BRAIN ACTIVITY AND EEG OSCILLATIONS WITH A REALISTIC HEAD MODEL

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Our objective was to model scalp EEG and brain oscillations with a hypercolumn level cortical resolution. We used a 3-D FEM model of an adult male subject constructed from 192 segmented axial MR slices with 256×256 pixel resolutions. The FEM voxel resolution was 1×1×1 mm. Majority of the tissues were identified that included: scalp, fat, muscle, dura layer, CSF, cerebellum, gray and white matter, and hard and soft skull bone. The electrical conductivities of various tissues were obtained from the literature. The electrical activity of the whole cortex was represented by 144,000 distributed dipolar sources with orientations normal to the local cortical surface. Each cortical voxel represented the electrical activity of a hypercolumn. The dipole intensity distribution in the whole cortex was in the range of 0.0 to 0.4 mA meter with a uniform random distribution. Using an adaptive FEM solver the potential and flux distributions in the whole head model were computed and scalp EEG were extracted. The spontaneous brain activity was modelled as a Gaussian i.i.d. random process. Its 1/f2 slope of the power spectral densities (PSD) was matched with the PSD computed from the measured 256 channel scalp EEG data of the subject by use of iterative optimization techniques. In addition, thalamo-cortical oscillations in theta, alpha and low

gamma bands were superimposed on the spontaneous brain activity by use of a neural mass model. Spatiotemporal contour plots of potentials on the scalp surface (EEG) were made. The PSD of simulated EEG exhibited a 1/f2 slope with broad peaks in theta, alpha and low gamma bands. These results suggest that it is feasible to simulate spatiotemporal characteristics of scalp EEG with a whole head model that included a detailed physiological modelling of the cortical electrical activity.

P3-001

GENETIC AND ENVIRONMENTAL INFLUENCES ON LINGUISTIC CEREBRAL FUNCTION IN ELDERLY TWINS USING MEG

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Aim: A genetic influence has been suggested for many cerebral functions, but little is known about language function. To estimate the genetic influence on the cerebral function during a language task, we used MEG to investigate the similarity of the cerebral oscillatory changes in elderly monozygotic twins.

Methods: This study evaluated 55 native Japanese speakers, including 19 monozygotic twin pairs. We measured the brain activity during a verb generation task using a 160-channnel whole-head MEG system. We investigated the spatio-temporal distribution of task-related cerebral oscillatory changes (ERS/ERD) using adaptive spatial filtering and a group statistical analysis. After detecting the peak coordinates of the ERD at 25-50 Hz, we estimated the power of the ERD in the peak coordinates using a time-frequency analysis. To compare the similarities in the power of the ERD within twin pairs, the correlation coefficient between the powers of the members of each twin pairs was determined. To compare twin pairs to unrelated subjects, we determined the correlation coefficient for 19 pairs of randomly drawn unrelated subjects.

Results: The peak of the ERD at 25-50 Hz was estimated in the left frontal area based on the group statistical analysis. The ERD first appeared in the 200-400 ms post-stimulus window and was sustained until 1600-1800 ms. In the peak coordinate, the power of the ERD showed a high correlation among twin pairs. The correlation coefficient was 0.54 in the 800-1000 ms period at the maximum. On the other hand, unrelated subjects had a lower correlation in all time windows.

Conclusion: We found that there was high similarity of the ERD of the left frontal area in elderly monozygotic twins. This finding suggested that the cerebral activity in left frontal area during a language task is under genetic influence.

P3-002

SPATIO-TEMPORAL DYNAMICS OF SYNTACTIC AMBIGUITY COMPUTATION

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The involvement of a left-lateralized fronto-temporal network in the computation of syntax has been demonstrated using functional magnetic resonance imaging (fMRI). In particular syntactic ambiguity and its resolution have shown to elicit a response in both the left inferior frontal gyrus (LIFG) and left posterior middle temporal gyrus (LpMTG). However, the electrophysiological temporal dynamics and connectivity in this network cannot be fully assessed using fMRI alone. We use magnetoencephalography (MEG) to independently characterize the network involved in this kind of syntactic computation. Using MEG's temporal advantage, we extend the spatial results to characterize the network dynamics. Thirteen right-handed participants (age range 19-29 years) were scanned using MEG while listening to phrases with a syntactic ambiguity (e.g. "landing planes"). At the end of each phrase a disambiguating verb was presented and the participants were asked to decide if the continuation was acceptable or unacceptable. In order to analyze the resolution of the syntactic ambiguity, minimum norm was used to localize the MEG data at the onset of the disambiguating verb. The time courses from regions of interest were extracted to compute connectivity and directionality measures. The resulting network indicated involvement of the LIFG and LpMTG with significant overlap in spatial structure to the network found independently using fMRI. Extending our analysis into the time domain, activity was first observed in the LpMTG before LIFG. Connectivity analysis suggested significant communication between these two regions demonstrated by strong phase locking values. Our results also suggested LpMTG drives LIFG in a Granger sense. These findings support the left hemispheric fronto-temporal model in syntactic computations and further establish the LpMTG and LIFG as important nodes in this network. Our results establish a neurobasis of the hemodynamic network found previously and characterizes the mechanisms involved in the resolution of syntactic ambiguity in this fronto-temporal network.

P3-003

INCREASING NETWORK SYNCHRONIZATION IS ASSOCIATED WITH THE DEVELOPMENT OF LANGUAGE ABILITIES

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The synchronization of oscillations among brain areas is understood to mediate network communication supporting cognition, perception and language. How task-dependent synchronization during expressive language processing develops throughout childhood and adolescence, as well as how such network coherence is related to the development of language abilities, remains poorly understood. To address this, we recorded MEG while 73 participants aged 4 – 18 years performed a verb generation task. Activity from 90 seed locations,

corresponding to all cortical and subcortical regions in the AAL atlas, was reconstructed using beamformer analysis. Phase synchronization was then calculated between all region pairs using the phase lag index (PLI). Graph analysis was used to characterize network connectivity. Psychometric tests were used to assess abilities in language and non-language domains. Task-dependent increases in synchronization were observed in the theta, alpha and beta frequency ranges, and network synchronization differences were observed between age groups (younger children, older children and adolescents). Task-dependent synchronization was strongest in the theta band, as were differences between age groups. Graph properties indexing network connectivity involving brain regions associated with verb generation were significantly associated with both age and language abilities. These findings establish the maturational trajectory of network synchronization underlying expressive language abilities throughout childhood and adolescence, and provide the first evidence for an association between large-scale network synchronization and individual differences in the development of language abilities.

P3-004

EARLY DIFFERENCES IN SEMANTIC PROCESSING DURING VISUAL NAMING: A MEG STUDY

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Visual naming involves a wide range of cognitive processes that are fundamental for speech, the cortical dynamics of which have yet to be fully described. We contribute to this description using an picture naming task in MEG, in which we manipulated the semantic demands across conditions.

In different blocks, participants overtly named: colours from random scrambled patches, line drawings of items from a single semantic category (vehicles), or line drawings of items from four categories. Colour naming demands the least semantic processing, while items from a single category target a smaller semantic "target-space" than items from multiple categories.

MEG data were collected on a 4D Neuroimaging system from seventeen subjects, of which two were excluded due to atypical levels of artifactual noise. The continuous signals were band-pass filtered between 0.5 and 35Hz and ERF amplitudes were averaged by subject and condition. Sources were reconstructed on the cortical surface of the MNI template using a Minimum Norm estimates. We performed time-resolved statistics on the source data using pair-wise planned comparisons (Student's t; $p < 0.001$ uncorrected).

Significant differences began in occipital cortex 54ms post stimulus, and spreading forward to anterior (R = 117, L = 318) and middle (L = 153ms, R = 122ms) bilateral temporal cortices, left temporo-parietal junction/inferior parietal lobule (232ms), left superior temporal cortex (330ms), bilateral IFG (L = 427ms, R = 232ms), among other significant differences in activity.

These regions are associated with visual object recognition, semantics, lexical retrieval, phonology and representational integration. The contrasts reveal early differences in the diffusion of information through a wide network. Notably, effects present in temporal cortices as early as 117 ~ 153ms post stimulus indicate early semantic processing. Reported differences are all present several hundred milliseconds before response onset, before movement-artifact related contamination of the recordings.

P3-005

MEG ASSESSMENT OF EXPRESSIVE LANGUAGE IN CHILDREN EVALUATED FOR EPILEPSY SURGERY.

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An important step in the presurgical evaluation of patients with medically refractory temporal lobe epilepsy is to reliably determine hemispheric language dominance. In the absence of a universally accepted gold-standard method to assess language dominance in preoperative assessment of patients a range of tools and methodologies have been explored, including magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) (Abou-Khalil, 2007). MEG has an advantage over methods such as fMRI as it relies on direct measures of brain electromagnetic processes and therefore has better temporal resolution. It is also insensitive to the effect of anatomical lesions on brain microvasculature. In this study we used MEG to investigate the reliability of indices of laterality of cortical activation during an expressive language task in a group of children evaluated for surgical treatment. Reliability of MEG data was assessed by direct comparison with intracranial electrical stimulation. Nine children with drug-resistant epilepsy, who were assessed for surgical amenability at the Birmingham Children's Hospital NHS Foundation Trust, participated in the study. Patients were recorded in a magnetically shielded room using an Elekta-Neuromag TRIUX 306 channel whole-head MEG system (Helsinki, Finland). The patients were asked to perform a verb generation task. All of the patients were able to perform the task successfully, with at least 95% of the stimuli correctly completed. The verb generation task was associated with decreases in the 15-25 Hz frequency band in regions of the left frontal lobe in all patients. Laterality index was computed in the 15-25 Hz range and was consistent with hemispheric dominance established with cortical stimulation. This study – albeit on a limited and selected clinical group - confirms that MEG is an important non-invasive method that can be used to assess cortical function and has significant potential to contribute to the routine assessment of surgical planning for patients.

P3-006

DEVELOPMENTAL CHANGES IN EXPRESSIVE LANGUAGE NETWORK CONNECTIVITY

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Introduction: Noninvasive neuroimaging consistently shows that children have diffuse language networks which become increasingly left-lateralized and focal with age. However, developmental changes in network connectivity have not been characterized. Here, we assess age-related changes in functional and effective connectivity for 21 children (5-19 yrs) completing a verb generation task in MEG (Kadis et al., 2011).

Methods: Data were collected at 625Hz, using a 151-channel CTF system, and analyzed using FieldTrip and SPM8. Recordings were noise corrected, bandpass filtered (0.1-100Hz), then coregistered to MRIs for singleshell head model construction.

The verb generation task engages bilateral inferior and middle frontal cortex in children. We used the WFU_PickAtlas and Talairach_Daemon to identify centroids of left and right BA44, BA45, and BA46. Virtual sensors were computed at each location using an LCMV beamformer.

Functional connectivity (coherence) among regions was computed from Fourier transformed data; effective connectivity (Granger causality) was computed from multivariate autoregressive models.

Results: Group functional connectivity analyses revealed two distinct clusters, reflecting left and right sensor pairings. We observed developmental decreases in coherence among ipsilateral pairs, but not contralateral pairs, across frequencies. We observed significant age-related decreases in delta (r=-0.647), theta (r=-0.632), and beta (r=-0.640) coherence between left BA44 and BA46 (FDR corrected, q=0.05).

Effective connectivity analyses revealed a dominant driver in left BA44 (Broca's) to ipsilateral BA45 and BA46. We observed developmental decreases in Granger causality between ipsilateral and contralateral sensor pairs, across frequencies; however, these correlations failed to survive correction for multiple comparisons.

Conclusion: Verb generation is supported by distinct subnetworks of the left and right frontal cortex, in childhood. Age-related decreases in functional connectivity suggest that the left lateralized, focal adult language network emerges from progressive disengagement of extracanonical areas (e.g., BA46).

P3-007

LANGUAGE-MOTOR INTERFERENCE REFLECTED IN BETA OSCILLATIONS

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According to embodied cognition theories, the involvement of the brain's motor system in action-related language processing can lead to overt interference with simultaneous action execution. The aim of the current study was to find behavioural and neurophysiological evidence for this interference effect using beta oscillations (15-25 Hz) measured by MEG.

Nineteen subjects performed concrete/abstract decisions on single verbs describing actions performed with the hands or the feet (i.e., concrete verbs), and abstract verbs. Button press responses with the right index finger indicated concrete verbs. Longer response latencies were expected for hand compared to foot verbs, reflecting interference effects. Beta oscillations were analysed using Fieldtrip (Oostenveld et al., 2011) to compare spectral power between conditions. The sensors of interest were defined by the significant channel cluster in a separate functional localizer task consisting of self-paced button presses.

Interference effects were found in the interaction of verb effector with imageability: while hand and foot verbs with low imageability were processed equally fast but slower than highly imageable verbs, response latencies for highly imageable hand verbs were longer than for highly imageable foot verbs.

This behavioural interference was accompanied by differences between conditions in the pre-movement beta-band power suppression between word onset and response execution. Beta suppression was significantly smaller for highly imageable hand verbs compared to highly imageable foot verbs at several time-channel clusters, as revealed by both stimulus-locked and response-locked analyses.

The behavioural results indicate that a beneficial influence of higher imageability on action verb processing time is perturbed when verb and motor response relate to the same body part. The beta-band effect provides additional neurophysiological evidence for language-motor interference: hand verb processing in cortical hand motor areas interacts with the typical beta suppression seen before movements. These findings support the embodied cognition hypothesis of motor simulation during action-related language processing.

P3-008

DECODING THE SEMANTICS OF WORDS IN ACTIVE AND PASSIVE SENTENCES FROM NEURAL ACTIVITY

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Previous work has shown that corpus-derived semantic feature representations for single words and phrases can be successfully decoded from brain imaging data using machine learning techniques (Murphy 2012, Mitchell 2008, Fyshe 2013); however, their application to sentence-level reading remains relatively underexplored. In this magnetoencephalography (MEG) study, participants read 16 active sentences (e.g. The dog found a peach) and their passive equivalents (e.g. A peach was found by the dog.), comprised of 16 total content words that were utilized multiple times to create 4 sentence contexts for each content word. Each sentence was presented for 15 repetitions, yielding 60 repetitions for each content word per condition. We created an independent measure of word semantics by dependency-parsing word usage patterns from a 16 billion word corpus and then compressing the resulting matrix to form a "semantic vector" for each word. We trained independent L2-regularized regressors to predict each semantic vector dimension as a function of the MEG data, using 50 repetitions to train and the average of the held-out 10 to test. The full set of 16 words that comprised the sentences were ranked by their cosine distance to the

semantic vector predicted for the held-out brain image. We report rank accuracy: the percentage of words amongst the 16 with cosine distance larger than the distance to the correct word. Results indicate that verbs and patients (e.g. peach in the above examples) were significantly more decodable when placed in Active-voiced sentences. Of further interest, verbs were not only decodable during their initial visual presentation, but also during the rest period immediately following the end of the sentence, perhaps reflecting a component of post-sentence integrative processing.

P3-009

MEG-DERIVED NEURAL OSCILLATORY ACTIVITY DIFFERENTIATES SENTENCE PROCESSING FROM WORD LIST PROCESSING IN THETA, BETA, AND GAMMA FREQUENCY BANDS ACROSS TIME AND SPACE

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The role of oscillatory neural activity has received less attention in studies of language processing compared to event-related activity. Oscillations may provide new insights into how the brain processes language because some involved subprocesses may not be strictly time- and phase-locked, and therefore not picked up as event-related activity. Here, we used magnetoencephalography combined with frequency domain beamforming to explore the spatiotemporal dynamics of oscillations in sentence processing. We presented sentences (Sent) and word lists (List; scrambled sentences) visually, word-by-word, to 102 subjects. We used the FieldTrip toolbox for analysing each word (-0.2–0.5 s, around word onset), from 2.5–100 Hz. We quantified the effects by computing the power difference between conditions, and used a non-parametric permutation test for statistical inference.

We observed Sent < List ($p < 0.001$) in the theta and beta bands (centred at 7.5 and 16 Hz, respectively), between 0.3–0.5 s after word onset. Effects in both frequency bands localised to the bilateral occipito-parietal and left frontal cortices; only theta localised to the middle temporal cortex. In the gamma band, we observed Sent > List ($p < 0.001$) at 50–60 Hz and 80–90 Hz. These effects localised to left occipital, parietal, frontal, and middle/superior temporal cortical areas, and varied in time for each region. We further quantified the power difference as a linear function of word order and observed Sent < List ($p < 0.001$) in bilateral occipital, temporal, and parietal regions in theta and beta.

The results revealed a number of regions beyond the classical language areas, suggesting that the differences between sentence and word list processing do not merely reflect lexical-retrieval and integration. In combination with the spectral specificity of the effects, our data suggest that top-down attentional processes, and bottom-up information processing are also differentially affected.

P3-010

LANGUAGE LATERALITY INDICES FROM TWO MEG TASKS AND THE COMPARISON WITH FMRI RESULTS FOR THE SAME PATIENTS WITH LEFT LANGUAGE DOMINANCE

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Although MEG has been clinically used to determine hemispheric language dominance during preoperative evaluations, different language tasks may result in different spatial-temporal brain activation patterns which might alter the language laterality calculation in various ways. Recently we developed a method to calculate laterality index (LI) for different brain regions of interest (ROIs) and demonstrated that the procedure of adding spectrally-match noise control stimuli to a well-studied passive auditory word-listening task (CRM) can improve MEG-based LI calculations. In this study we applied the same LI calculations to an overt definition naming (DN) task with similar noise control stimuli. Then we compared the LIs from the CRM as well as the DN task against the LIs calculated from a classical semantic decision/tone decision fMRI task for the same patient cohort. We studied 7 epilepsy patients with left language lateralization from all three tasks. Our analysis shows that the best correlation between MEG-fMRI tasks comes from the DN LI from the inferior parietal/supramarginal ROI when correlating with the fMRI LI from the angular ROI, followed by the DN LI from the same ROI when correlating with the fMRI temporal ROI. LIs of Frontal ROI from CRM or DN has a low correlation with LI of fMRI Frontal ROI, and the CRM LIs tend to correlate less well with the fMRI LIs than the DN LIs for this patient cohort.

P3-011

TRACKING CORTICAL LANGUAGE PROCESSING STREAMS WITH NAVIGATED TMS

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Interhemispheric specialization and interaction have been investigated by measuring reaction times (RTs) in lexical decision tasks. Several studies have shown a right-visual-field advantage (RVFA) in reaction times and/or accuracy for right-handed subjects. This suggests that the left hemisphere (LH) is specialized for linguistic information processing. Two models could explain the RVFA. In the callosal relay model, the right hemisphere (RH) does not process the linguistic information it receives, but the information is relayed through the

corpus callosum to the LH; RVFA is explained by the time needed for the signal to propagate to the language-dominant hemisphere. In the direct access model, the RVFA occurs because the left-visual-field information is processed slower in the non-dominant RH. To the authors' knowledge, neither of the models has yet been proven to outweigh the other.

In this study, navigated transcranial magnetic stimulation (TMS) was applied during a hemifield lexical decision task in both right-hand- and left-hand-response conditions; RTs and error rates were measured. The main hypothesis was that TMS to a language-related LH site yields different RTs compared to the no-TMS condition, whereas TMS on the homologous RH site should not affect performance. In addition, several sites, e.g., Broca's and Wernicke's areas and their right-side homologues, were stimulated to evaluate whether they belong to the essential processing stream needed for lexical decision. Frequent four-letter Finnish words and non-words were presented in one hemifield at a time.

The preliminary results suggest that, first, there are RT differences between different hemifield and hand conditions, and second, TMS on Broca's area is able to affect the subject's performance in the hemifield lexical decision task. More subjects and cortical sites will be measured to further evaluate the models.

P3-012
MEG ACTIVITY FOR PHONOLOGICAL AND SEMANTIC RESOURCES IN VERBAL SHORT-TERM MEMORY

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Repetition of sentences depends on two distinct forms of verbal short-term memory: phonological and semantic, but the nature of these resources is uncertain. We designed a novel behavioural paradigm to examine the mechanisms that support immediate repetition of sentences, and their encoding into long-term memory, using short-term sentence repetition and a subsequent cued recall task, in which subjects recalled sentences based on two-word cues. This paradigm was used first in a behavioural experiment, and then in a MEG study.

The behavioural experiment examined competitive interactions between phonological and semantic maintenance by manipulating the degree of phonological interference during a delay period for sentence repetition. Blocking rehearsal reduced accuracy for immediate recall, but ultimately enhanced long-term memory (LTM) for the same sentences in cued recall. We propose that semantic resources are recruited as needed to support short term recall, and these promote encoding into LTM.

In the MEG experiment, subjects repeated abstract or concrete sentences, or word lists, immediately following a five-second unfilled delay. Oscillatory neural activity was mapped with Synthetic Aperture Magnetometry. Subsequent cued recall was assessed after MEG. Retention of sentences induced widespread power decrease in the alpha and beta bands (8-30 Hz, associated with neural activation), in the left hemisphere. Retention vs. listening specifically activated dorsal frontal-parietal regions. Retaining word lists induced additional activation in bilateral dorsal regions. Concrete sentences preferentially activated ventral temporal regions. Right hemisphere frontal-parietal regions were selectively engaged for sentences that were ultimately forgotten, rather than remembered. Word lists and poorly remembered sentences also induced increased frontal midline theta power. We propose that bilateral dorsal regions contribute to phonological maintenance of verbal material in more demanding conditions, but do not promote long-term encoding. The same is likely true of frontal theta. Semantic maintenance appears to involve bilateral temporal regions.

P3-013
PHONOLOGICAL DISORDERS IN DYSLEXIA: MEG EVIDENCE FOR IMPAIRED CONNECTIVITY

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Poor speech processing skills have been observed in dyslexic readers: reading abilities are, in fact, highly correlated with phonological awareness. However, it is not clear if such behaviourally observable deficits are due to basic difficulties in speech perception or to the metalinguistic nature of the employed paradigms involving conscious decisions. Available neurophysiological data do not provide clear evidence, since few studies focused on the neural networks whose brain oscillations couple with natural speech.

Dyslexic participants (N=10; mean age: 31 ± 5.3) and controls (N=10; mean age: 32 ± 5.3) listened to sentences for comprehension. We computed the spectral coherence between the speech signal and the MEG recordings collected during either speech listening or resting state at multiple frequencies.

We observed significantly higher coherence values during listening both in the 0.5-1 Hz and 5-7 Hz frequency bands. Group differences however only emerged at 0.5-1 Hz. Source reconstruction in this frequency band (Dynamic Imaging of Coherent Sources, for all participants) revealed increased coherence for speech listening compared to resting state in a bilateral peri-sylvian network. Coherence values were significantly reduced for dyslexic participants in the right auditory cortex and the left inferior frontal gyrus (pars opercularis).

Functional connectivity (seed-based Partial Direct Coherence) computed from brain oscillations in this frequency band revealed a distributed network of bidirectional connections. Dyslexics (vs. controls) however presented significantly hampered connection from the right auditory cortex towards left inferior frontal regions. Strength of this connection significantly correlated with both reading measures and phonological awareness ratings.

We support the claim that natural speech sampling (at low frequencies) is impaired in dyslexic readers. In addition, we propose that phonological disorders can be explained as a disconnection syndrome due to impaired information flow from perceptual cortices to regions implicated in high-level manipulation of phonological information.

P3-014

VALIDITY OF DETERMINING LANGUAGE LATERALITY USING TRANSCRANIAL MAGNETIC STIMULATION: COMPARISON WITH MEG AND CORTICAL STIMULATION

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Transcranial Magnetic Stimulation (TMS) was recently approved by the FDA for use in presurgical mapping of motor and language regions in the vicinity of a tumor or an epileptiform focus. We investigated if TMS can also be used to establish language laterality. We attempted langauge laterality determination with TMS and MEG in 40 patients (22 females) with epilepsy or brain tumors (mean age 21 years, range 8 – 52 years) referred to our institution. Patients were assessed in MEG for receptive language using continuous auditory word recognition paradigm and their expressive language was assessed with navigated TMS while they performed a naming task. Language laterality was determined successfully by each modality in 33 patients, and by both modalities in 26 patients. Of the 26 patients in whom both MEG and TMS were successful, laterality was concordant in 21 patients (20 left and 1 bilateral). Laterality was deemed to be bilateral by TMS and left lateralized by MEG in 3 patients, and the laterality was reversed in 2 patients. TMS was successful in determining language laterality in seven patients in whom VNS artifacts prevented successful mapping with MEG, while in 7 different patients who could not tolerate TMS stimulation language laterality was determined successfully with MEG. The language areas in the inferior frontal gyrus identified by TMS were verified by cortical stimulation mapping (CSM) during subdural grid electrode stimulation in 4 patients. All patients tolerated TMS with no serious adverse effects. Our data indicate that TMS was in good agreement with MEG in identifying langauge laterality (80%), and the localization of Broca's area by TMS was confirmed by CSM. Hence, TMS is a safe and reliable alternative to MEG in determining langauge laterality especially in patients with VNS, dental fillings or metal in the body.

P3-015

NEURAL DYNAMICS OF VISUAL WORD RECOGNITION

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Visual word recognition is a complex task which is critically dependent on efficient interactions between visual and non visual processes. Previous coherence analyses between source Magentoencephalography (MEG) estimates have identified a widely distributed and densely interconnected network of brain regions that are associated with reading (Kujala et. al. Cerebral Cortex 2007; 17:1476-1485).

The present study develops these findings by investigating the the direction of information flow within the reading network and how this changes over time. Seven particiapants completed 1500 trials of a single word (of high, medium or low word frequency) one-back task during a high sample rate MEG recording.

Delay and dimensionality parameters for a time delay embedding were objectively assessed across source current flow estimates within the reading network within short, densely overlapping time-windows spanning the stimulus presentation time. This embedding was subsequently used as a predictor for future activity in a MultiVariate AutoRegressive (MVAR) model. Separate models were fitted for the low and high frequency words before Partial Directed Coherence (PDC) was used to characterise interactions within the network in the frequency domain. Non-parametric permutations were used to establish connections which were significantly different when reading high or low frequency words.

Overall, our results suggest that visual word recognition is subserved by a complex pattern of interactions which vary over both time and frequency. Moreover this network demonstrates extremely rapid parallelization throughout the network from its entry point at the occipito-temporal cortex.

P3-016

INTEGRATING LEXICAL-SEMANTIC FEATURES AT DIFFERENT CORTICAL SCALES: A DISSOCIATION BETWEEN THETA AND GAMMA OSCILLATIONS IN THE ANTERIOR TEMPORAL LOBE

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Research from the previous decade suggests that word meaning is partially stored in distributed modality-specific cortical networks. However, little is known about the mechanisms by which semantic content from multiple modalities is integrated into a coherent multisensory representation. The current study used magnetoencephalography (MEG) to investigate changes in oscillatory neuronal activity while participants verified two features for a given target word (e.g., BUS). Feature pairs consisted of either two features from the same (visual: big-red) or different modalities (audio-visual: loud-red). The results suggest that semantic integration at a local scale (modality-specific) is associated with enhanced high-frequency power (80-120Hz), while integrating information at a global scale (cross-modal) is associated with a sustained increase in low frequency power (2-8Hz). Source reconstruction revealed a peak in the anterior temporal lobe (ATL) for both low- and high-frequency effects. Taken together, the data suggest that a) oscillatory activity is sensitive to the scale at which semantic information is integrated and b) the temporal dynamics within the ATL could be informative as to how this region contributes to the integration of semantic information.

P3-017

IMPACT OF COCKTAIL PARTY NOISE ON THE DYNAMIC MODULATION OF AUDITORY BETA-BAND OSCILLATIONS BY VOICE POWER

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Introduction: During continuous speech listening, listener's low β-band (βlow, 13–20 Hz) oscillations in bilateral superior temporal gyri (STG) are dynamically modulated (in a speech-sensitive manner) by the speaker's voice power, βlow oscillations being reduced when the voice power increases and vice-versa (Bourguignon et al. in preparation). These amplitude modulations are paced by speech temporal envelope at ~0.5 Hz. Here, we investigate the impact of a fluctuating background noise on the dynamic modulation of listener's βlow oscillations.

Methods: Neuromagnetic activity of 20 right-handed and native French speaking adults (10 females, mean age 30 years) was recorded using whole-scalp MEG (Elekta) while they listened to five different recorded texts read in French by different native French-speaking readers. Recordings were mixed with a "cocktail party" type noise at different signal to noise ratios (SNR; No noise, +5dB, 0dB, –5dB, –10dB). Coherence between βlow envelope and speech temporal envelope was computed at 0.5 Hz for each subject and condition, using 2-s long epochs. Coherent sources were reconstructed using minimum norm estimate. Statistical significance of the coherent sources was assessed with surrogate-data-based statistics. The influence of the SNR on coherence level was assessed using one-way ANOVA.

Results: Without noise, significant coupling between βlow and speech power occurred in 18 subjects at bilateral STG (group-level source coherence, right STG: 0.025, left STG: 0.028). When speech merged into noise, this coupling significantly vanished ($p<10^{-6}$, ANOVA), with only 4 subjects showing significant coupling at +5 dB, 2 subjects at 0 dB and 2 subjects at –5 dB.

Discussion: This study demonstrates that a cocktail party background drastically reduces the coupling at 0.5 Hz between βlow and voice envelope fluctuations at the STG. These data are congruent with recent studies that showed reduced β-band suppression during speech-in-noise (Schepers et al., 2013).

P3-018

IS EYE-CLOSURE ALPHA RELATED TO MEMORY-SUCCESS ALPHA?

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One of the most heavily-studied effects in human electrophysiology is the alpha power increase that occurs when the eyes are closed (Berger, 1929). Some psychological studies have shown that eye closure can boost memory performance in certain circumstances. While previous studies have demonstrated that alpha power is modulated during different phases of memory tasks, and that these modulations are correlated with performance, most of them have used visual stimuli for the memory tests, and there are few existing reports on the relationship between eye closure, memory, and alpha-band power. Participants (n=19) in the present study performed a recognition memory task using auditory spoken words while MEG data was recorded. Half of the recognition trials were done with eyes open and half with eyes closed. Recall performance was equivalent for the eyes-closed and eyes-open conditions. Responses to the stimuli showed the expected alpha ERD 0.5-1 s after word onset. This ERD was modulated differently by remembered and forgotten words in temporal sensors, while eyes closure modulated alpha band power at occipito-parietal areas and did not affect performance. The different power spectrum topographies of the modulations and the lack of differences between eyes closed and eyes open during task, suggest that these rhythms play distinct functional roles in memory performance.

P3-019

NEUROFUNCTIONAL DIFFERENCES OF MILD TRAUMATIC BRAIN INJURY ELICITED DURING A WORKING MEMORY TASK

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Mild Traumatic Brain Injury (mTBI) is acquired brain damage from an external force, and is an international health concern. Whilst more severe categories of the injury often show anatomical abnormalities on CT scans, mTBI diagnosis is more difficult due to the absence of physiological changes on routine scanning. However, patients often report secondary cognitive sequelae as a result of mTBI, and the aetiology of such complaints are thought to derive from atypical neural functioning. MEG's exquisite temporal resolution may be able to provide insight into the neural basis of these cognitive deficits. Here, we used MEG to investigate memory processing in mTBI populations. We examined the neural differences between mTBI (n=17) and a healthy control population (n=19) in a working memory task (1-back). Whilst there was no significant difference in reaction time or accuracy, the mTBI group showed increased activation between 150-225 ms post stimuli onset in the right hippocampus and right insula relative to the controls during recognition trials. Right hippocampal activation has been shown previously in this task in healthy adults; these findings suggest that the mTBI group recruits additional neural resources to maintain comparable level of performance. This increased activation may reflect some of the secondary memory deficits experienced by those with mTBI. Furthermore, we found substantial differences in the visual evoked fields, with mTBI patients not exhibiting off-set evoked responses to the visual stimuli that were reliably seen in control participants. In other words, the rapidly (200ms) presented images induce ongoing suppression of

visual processing even after the image has disappeared. This finding could be of clinical relevance, as this visual evoked field is large enough to be measured at the single subject level and warrants further investigation into abnormalities of visual evoked fields in mTBI populations.

P3-020

IDENTIFYING THE MEG SOURCES THAT SUPPORT THE FORMATION OF SPATIOTEMPORAL MEMORIES

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Our memories of past events often contain many spatial details, including the location, point of view, and segments of pathways. Recently, it has been proposed that episodic memory is constituted not only by single snapshots of item-context associations, but also involves the encoding of full spatio-temporal trajectories (Hasselmo, 2008). Current computational models derived from rodent studies suggest that parallel processing in head-direction system and entorhinal cortex converge in the hippocampus, where these spatiotemporal experiences are finally formed. However, it is still unclear how these models apply to humans.

The aim of this study was to identify the major brain generators of oscillatory activity, relevant for the association of spatial information to episodic memories. We obtained MEG recordings from healthy young adults while they performed a navigation task in a computer-simulated arena, which included distal visual cues. Participants had to memorize the position and direction of different shops within the virtual environment. During the encoding phase, participants turned until facing a house that cued a particular location. Then, they moved to this location, where a picture of the shop was presented. After a distraction task, participants indicated the remembered location and direction of each shop picture. Curiously, midline-prefrontal theta activity (4-8 Hz) during the encoding of pictures predicted bigger location errors. However, power of a "slower theta" rhythm (2-3 Hz) during movement in the encoding phase was positively correlated with location accuracy. This effect was localized with DICS in right posterior hippocampus/parahippocampus, calcarine sulcus, and left inferior frontal gyrus.

Our results strongly suggest that the "slower theta" oscillation indicates binding of object-place information and is therefore essential for the formation of spatiotemporal memories in humans. Validation of medial temporal lobe findings with intracranial EEG is in progress.

P3-021

STATISTICAL LEARNING IN LANGUAGE ACQUISITION

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We investigated how the statistical learning in language acquisition is reflected in neuromagnetic responses. Vowel tones with fundamental frequencies in a five-tone equal temperament and five different combinations of the first and second formant frequencies were generated as a set of five Japanese vowels (a, e, i, o, and u) using a formant synthesizer. By combining three vowels out of five, the five different sequences (aue, oiu, eao, uoi, and iea) were created as nonsense words. These words were ordered with the constraint that the probability of forthcoming word was statistically defined (80% for one word; 20% for the other one) by the latest two successive words (second-order Markov chains) to form 600-word sequences. All of the word transitions in ratios (80% to 20%) in the first half were inverted in the latter half of the word sequences. Neuromagnetic responses to the word sequences were recorded from fourteen right-handed Japanese participants. Temporal profiles of the N1m responses to the three tones (initial, middle, and final tones) in the words ordered with higher and lower transitional probabilities were compared. In the first half, the N1m responses to the first tones in the word ordered with a higher transitional probability were significantly decreased compared with those with a lower transitional probability. Furthermore, regardless of the transitional probabilities, the N1m responses to the second and last tones were significantly decreased compared with those to the first tones, and this significant difference between the first tones and the other two tones were retained even after the word transitional probabilities were inverted. The N1m response may be useful as a marker for statistical learning in language acquisition. The two types of statistical learning for word segmentation and word connection may be performed in distinct stages of language learning.

P3-022

SPATIOTEMPORAL OSCILLATORY DYNAMICS DURING THE ENCODING PERIOD OF A VISUAL WORKING MEMORY TASK

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Many electrophysiology studies have examined neural oscillatory activity during the encoding, maintenance, and/or retrieval phases of various working memory tasks. These studies have contributed to current conceptualizations of the neural dynamics that underlie working memory functions, although much remains to be discovered. Moreover, several key findings in this literature have not replicated across different studies, and the origin of these inconsistencies is not understood. In the current study, we examined the neural processes that serve visual working memory encoding using high-density magnetoencephalography (MEG) in healthy adults while they performed a high-load, Sternberg-type working memory task. We used an entirely data-driven approach to identify the significant oscillatory responses that

occurred during the encoding phase of the task, and these responses were imaged using beamforming. Furthermore, we examined the dynamics of the encoding phase by imaging four non-overlapping 400ms time bins within a significant time-frequency component of the encoding phase, and statistically compared these distinct time windows. We found significant 9-16 Hz desynchronizations in the bilateral occipital cortices and the dorsolateral prefrontal cortex (DLPFC) that were sustained throughout the encoding phase. Our analysis of the dynamics showed that the DLPFC desynchronization was evoked later in the encoding phase relative to the occipital responses, which were strongest in the earliest stage of encoding and subsequently significantly decreased in amplitude thereafter. The DLPFC response, on the other hand, reached its peak in the second 400ms time bin, and then linearly increased concurrent with the decrease in occipital responses. These results provide evidence of dynamic network processes during the encoding phase of working memory. The presence of such dynamic oscillatory networks may be a potential source of the inconsistent findings in this literature, and supports the notion of an altered pattern of functionally discrete sub-processes within the encoding phase of working memory processing.

P3-023

SUSTAINED ACTIVITY IN HUMAN AUDITORY CORTEX DURING A WORKING-MEMORY TASK: AN MEG STUDY

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Working memory (WM) refers to the processes used for temporarily storing and manipulating goal-relevant information not currently available in the environment. To identify neural correlates of auditory WM in the human AC, we performed an MEG study in which we compared neuronal activity in a 'high-memory' condition and a 'low-memory' condition in a WM task. In the high-memory condition, subjects had to memorize the first stimulus, S1, of a pair of stimuli in order to solve the task, whereas in the low-memory condition this was not necessary. Persistent neuronal activity in the delay period between S1 and S2 is generally taken as the neural correlate of WM.

S1 and S2 were tones with frequencies A=1.5 kHz or B=1.6 kHz, separated by a delay of 2 s. In a given trial, one of the four possible different pairs (AA, AB, BA, BB) was presented. In a given block of trials, all pairs occurred in random order, but only AA constituted the target (Go stimulus), which the subject had to report by a motor response. To account for a possible confound due to their preparation for the motor response, subjects participated in a further experiment, in which they had to respond only when the first tone was A.

Analysis of the grand mean across 12 subjects revealed increased activity in the delay phase for the high-memory condition compared to the low-memory condition. This finding was statistically significant for sources located in the AC of the right hemisphere, irrespective of the ear of stimulation. Source activity in the delay phase of the high-memory condition was also larger in the left AC, but did not reach significance. The motor control task did not reveal any differences in the delay phase between target and non-target condition.

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P3-024

VIDEO-GAME NEUROFEEDBACK SYSTEM FOR TRAINING OF BRAIN MACHINE INTERFACE: A COMBINED EEG AND MEG STUDY

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Our purpose is to determine effective and efficient training procedures for event-related desynchronization (ERD)-related brain machine interface (BMI). To motivate subjects for training, we developed a motor imagery training system having videogame-like interfaces that gives subject an on-line visual feedback. We trained five healthy young-adult subjects using EEG and evaluated the training effect using MEG which has better spatial resolution over EEG. In the neurofeedback training, EEG signal was subjected to Fast Fourier Transform to determine feature vectors. We used Support Vector Machine to classify the feature vectors into any one of the states of (1) left or (2) right hand motor imagery or (3) rest. The classified result was fed back to the subject every 1 s as a cursor movement in the computer screen, and subjects got points when they successfully moved the cursor to catch an object that was falling down from the top of the screen. We calculated the total score on each training day and utilized them as the indices of their accuracy in BMI training. Five days of neurofeedback training significantly increased the total score in 3 out of 5 subjects; the average score increased from 0.33 ± 0.22 to 6.7 ± 1.2 in these subjects (15 for 100% success). ERD during finger tapping in one of these subjects who showed significant improvement of BMI control was further determined using MEG to investigate whether successful separation of brain oscillatory pattern over the states of intended movements and rest was developed by training. Time-frequency analysis demonstrated that power spectrum of μ rhythm (10-12 Hz) during finger tapping significantly decreased against rest period (2.0~2.5 s before tapping; $p<0.05$) at channels corresponding to the primary motor cortex contralateral to the movement side. MEG is capable of quantitatively estimating the plastic change of brain and therefore helps determining effective training method.

P3-025

WORKING MEMORY ABILITY ASSOCIATED WITH LOAD-DEPENDENT DESYNCHRONY IN INFERIOR PARIETAL AND PRECUNEUS REGIONS DURING AN N-BACK TASK

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Aims: To uncover neuromagnetic activity underpinning inter-individual variability in working memory (WM) performance.

Methods: Eighty-five (31M) native English speakers (Age: 23.6years (3.43)) completed the MATRICS Consensus Cognitive Battery (MCCB) and WM

scores were derived. In a separate session, they completed an n-back task in a CTF MEG device. Numbers 1-4 were visually presented at a rate of 1 per 2.3s. Participants completed 6 blocks of 10 trials for each of 0-, 1-, and 2-back conditions, making button-press responses to indicate respectively the number presented in the current, previous, or 2 trials previously.

Load-dependent group-level changes in response magnitude within classical frequency bands were localised via a SAM beamformer. Guided by these images, locations of peak responses for each individual were identified and used to construct virtual sensors (VS), from which mean magnitude change for pairwise contrasts between conditions were extracted. Step-wise linear regression was used to identify which VSs for each load contrast were predictive of MCCB WM performance.

Results: Significant WM load modulations included: desynchrony in bilateral parietal (4-8Hz), precuneus (8-13Hz) and left primary motor (13-30Hz) cortices and synchrony in bilateral frontal (4-8Hz, 60-90Hz) areas. WM percentile scores had a mean of 57.23 (SD=23.32). Higher scores were predicted by lesser right precuneus desynchrony at 8-13Hz for 1-vs0-back (β=.404, p<.001) and greater right parietal desynchrony at 4-8Hz for 2-vs0-back (β=-.321, p=.001). Model R^2=.167; $F(2,79)$=7.92, p=.001.

Conclusions: Greater inferior parietal recruitment with increased load, perhaps associated with attentional mechanisms[1], predicted higher WM ability. Conversely, greater precuneus desynchrony was linked with poorer WM performance, possibly reflecting greater disruption to default mode networks [2].

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P3-026

SLEEP-DEPENDENT CHANGES IN LEARNING-RELATED MAGNETIC EVOKED FIELDS IN CHILDREN

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Behavioural studies have highlighted a beneficial impact of post-training sleep on the consolidation of declarative memories in children. However, the underlying cerebral mechanisms remain barely investigated, despite their relevance for the understanding of associations between cognitive impairment and abnormal sleep activity in developmental disorders. In the present study, we used magnetoencephalography (MEG) to investigate the impact of a 90-minutes diurnal sleep (nap) on the sleep-dependent brain processes subtending memory retrieval after learning functional properties of novel objects, i.e. a core mechanism in the development of conceptual, cognitive and declarative knowledge in children. Twenty-one healthy children were scanned using magnetoencephalography (MEG 306-channel, Vectorview, Elekta Oy, Finland) during three picture-definition sessions, i.e. pre-learning [session 1; S1], immediate retrieval [S2] and delayed retrieval [S3]). S2 and S3 were separated by either a 90-minutes nap (Sleep group; S) or a similar period of wakeful rest (Wake group; W). Children were randomly assigned between conditions. After MEG data preprocessing (band-pass filtering 0.5-40 Hz, epoching -200:1200 ms, baseline correction -200:0 ms, head-movement/ ICA artifact rejection), immediate (S2) vs. delayed (S3) retrieval Event Related magnetic Fields (ERFs) were compared between groups, first in sensor then in source spaces. Although similar behavioural patterns were observed in W and S participants at S2 and S3, results in sensor space disclosed a sleep-dependent ERFs modulation for newly learned non-objects, developing 450-650 ms after stimulus onset (p_{corr} <.05). Analyses in the source space windowed over this late temporal component of interest disclosed underlying activity in the left medial prefrontal cortex (-12,40,-12; p_{svc} <.05), in a location previously associated (using fMRI) with long-term overnight storage of verbal declarative memories. Altogether, our results suggest that sleep in children like in adults subtend memory consolidation and a sleep-dependent functional reorganization of learning-related brain circuits.

P3-027

READING WHAT'S ON YOUR MIND: DECODING IMAGES OF DIFFERENT CATEGORIES FROM WORKING MEMORY MAINTENANCE

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Working memory is a process that has been associated with sustained neuronal activity during maintenance. Furthermore, neuronal oscillations have been shown to be modulated in various working memory tasks. However, it is unclear whether these oscillatory modulations reflect general memory processes, or whether they reflect the maintenance of working memory in a representation-specific manner.

In this study, a working memory task was used in which subjects were sequentially presented with two images from different categories. These categories were faces, handwritten letters, and tools. The subjects were then instructed by a cue to only maintain the first or the second image. In some trials, subjects were instructed to maintain both images. Our design allows us to exclude that effects found during the maintenance period could be attributed to the visual presentations per se.

Using an elastic net classification algorithm, we could reliably decode whether the cued item retained in memory was a face or a letter. Power in the alpha band originating from the posterior part of the brain was of importance in making this distinction. Also power in the theta band over frontal and central regions, as well as posterior beta power contributed to the accuracy of the classifier.

We then assessed the representation-specific activity over time, by studying the classification accuracy over subsequent time bins of the delay interval. Classification was most reliable during the first few seconds of the delay period before returning to chance level.

These results demonstrate that the maintenance of working memory items is associated with representation-specific activity in the theta, alpha and beta band.

We are currently investigating the temporal dynamics of maintaining two items in memory, as well as to what extent the classification rate is modulated in a phasic manner by theta and alpha oscillations.

P3-028

GAMMA OSCILLATIONS UNDERLIE THE MAINTENANCE AND INTEGRATION OF FEATURES IN VISUAL WORKING MEMORY

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Visual working memory (VWM) holds visual information "online" for a short period as integrated object representations. In visual perception, gamma-band synchronization may provide a relational code for binding feature-specific neuronal assemblies into such representations. Recent studies show that both large-scale and local beta- and gamma-band synchronization characterize VWM retention and predict task performance. Although VWM content-specific synchronization has been observed in monkey fronto-parietal regions, the role of gamma oscillations in the maintenance of visual features remains unclear.

To investigate VWM feature-specific neuronal oscillations, we used M/EEG recordings and a match-to-sample task where the subjects memorized stimuli with either single features (shapes, colours, or locations) or conjunctions of colours and locations of two or four objects. Cortically-constrained minimum-norm estimates and individual surface source models were used to reconstruct the phase and amplitude time series of 400 cortical parcels. We computed source oscillation amplitude dynamics, all-to-all inter-areal phase-synchrony, and cross frequency phase-amplitude coupling across 31 frequency bands (3~120 Hz). All results were FDR corrected. We found that sustained memory-load dependent enhancement of gamma amplitudes during retention in feature-specific visual and prefrontal areas was specific to memorized features and pronounced for shapes and conjunction. Meanwhile, with load dependent local amplitude increase, despite broad-band amplitude suppression during VWM retention, long-range narrow-band synchronization in the alpha and gamma bands characterized VWM retention but was only slightly load dependent. Importantly, local gamma amplitudes were nested to alpha-band phase for all object features.

The dependence of gamma synchronization on feature-binding demands is in line with the hypothesis of gamma synchronization signalling the perceptual relatedness of features for coherent object representations. Our results provide evidence that gamma synchronization serves as a crucial mechanism in the maintenance of feature-specific information in VWM, and, together with large-scale alpha-band networks, underlies more general VWM functions.

P3-029

SERIAL-POSITION CURVE OF ALPHA-BAND AMPLITUDE SHOWN IN A SHORT-TERM MEMORY TASK

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When memory items are presented sequentially, the first and last items should be memorized well (primacy/recency effect). In order to clarify the mechanism of the effect, we recorded MEG alpha-band rhythm during memorization of sequentially presented memory items.

In the memory task, seven arrow images with 4 directions were presented randomly and sequentially. Afterwards, a recall number (1-7) was presented. Participants memorized the arrow direction in order and answered the direction that was presented at the order indicated by the recall number by pressing a button. The participants also took part in two control tasks: in Control 1, each participant was presented with arrow images in the same manner but pressed the button with the direction instructed previously, and in Control 2, the seven arrow images with the same direction were presented.

The correct rates against recall number showed a clear serial-position curve, i.e., primacy/recency effect. The alpha-band amplitude during memorization of the arrow images also showed a serial-position curve, in which the alpha-band during presentation of the first and last arrows was more suppressed. Hence, the alpha-band amplitude was inversely correlated to the correct rate. Sensors with significant correlation are distributed widely over the parietal and the bilateral regions, suggesting that these regions are associated with short-term memory. In addition, a correlation between alpha-band amplitude and correct rate, which was obtained in the memory task, was observed in Control 1 but not in Control 2. These results suggest that the primacy/recency effect arises regardless of the intention of memory. This is because a correlation was observed in Control 1, in which participants "could" memorize, while a correlation was not observed in Control 2, in which participants "could not" memorize.

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P3-030
LONG-TERM ARTISTIC TRAINING MODULATES ALPHA OSCILLATIONS IN THE INFERIOR FRONTAL GYRUS

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Artistic training is a complex learning that requires the meticulous orchestration of sophisticated polysensory, motor, cognitive, and emotional elements of mental capacity to harvest an aesthetic creation. Empathy and embodiment are critical constituents underpinning the holistic esthetic consciousness that enables an artist's work to resonate appraisal and appreciation [1]. Decreased alpha activity in the frontal cortex has been reported to relate the prosodic process [2] and semantic performance in fine artists [3]. In the current study, art school students majoring in painting, dancing, singing, piano, string instrument, and age-matched non-artist controls (20-30 for each group) were enrolled. Prosodic verbal stimulation, "hey," with different emotions (happy, sad, fear, angry, and neutral) was presented using optimum-MMN like design. The noise-free magnetoencephalographic (306-channel Vectorview, Neuromag) data were filtered at alpha band (9-13 Hz) followed by a beamforming source imaging method [4] to obtain cortical activity maps of evoked responses. We focused on brain responses at ~100 milliseconds after stimulus onset (M100). SPM8 and AAL were adopted for statistical image processing and anatomical labeling. A one-way ANOVA test was conducted in a voxel-wise manner ($F(2,38)=6.11$, uncorrected $p < 0.005$, cluster size = 30). A key finding was a group main effect of the M100 component in the left inferior frontal cortex (Brodmann area 45). We will present in this MEG report of the brain responses, particularly alpha oscillations, to prosodic verbal stimulation in students of various artistic forms to elucidate the domain general and domain specific issue in the context of stimulus-driven embodiment.

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P3-031
TRANSIENT AND BI-STATE LARGE-SCALE CONNECTIVITY IN SPONTANEOUS BRAIN ACTIVITY

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There is a very limited understanding of the dynamics of large-scale brain-wide correlation and how it arises mechanistically. We found that inter-regional correlations in spontaneous human brain activity are inherently bistable with periods of zero correlation interspersed with transient periods of heightened correlation, and that this is an emergent property of a weakly coupled network of oscillating brain areas. We used sliding window correlation approaches on the power of band-limited time courses from MEG data, and show that non-stationarity and bi-stability occur in the same brain areas and in the alpha to beta range (8-30Hz) as stationary measures of functional connectivity. We then developed a realistic large scale biophysical network model based on empirically-derived anatomical connectivity to simulate spontaneous brain activity. At moderately weak coupling strengths this produces spontaneous metastable oscillatory states with correlations in the alpha to beta range (8-30Hz), and, without any further tuning, exhibits the same frequency-specific non-stationarity and bi-stability observed in real data

P3-032
PHASE-SLOPE ANALYSIS REVEALS TOP-DOWN DIRECTIONALITY OF FRONTO-TEMPORAL COHERENCE IN OBJECT-BASED ATTENTION

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We studied the mechanisms that allow for top-down control of object-based attention by analyzing MEG signals from fMRI-guided regions of interest. When attending to either faces or houses in a spatially overlaid compound stimulus, an area in prefrontal cortex (IFJ) becomes selectively coupled with the respective sensory area in IT cortex (FFA vs. PPA). We tested the directionality of these interactions by analyzing phase lags between the functionally coupled oscillators. To disambiguate which of the two signals is leading we considered several narrow frequency bins around the peak frequency of maximal coupling. For each frequency bin, we subtracted the angle information of their Hilbert transform resulting in a phase lag distribution, which then was baseline corrected to disregard random phase relationships as well as electromagnetic field spread (at zero phase lag). When tracking the peak of these baseline corrected phase lag distributions over several frequency bins, a fixed transmission time between two sites translates into a linearly increasing phase-lead with increasing frequency ($\phi(f) = 2\pi ft$). The phase-slope analysis also allows estimating transmission times between the two areas. We found predominant top-down directionality with prefrontal cortex leading over IT cortex by about 20ms.

P3-033
ATTENTIONAL ENHANCEMENT OF AUDITORY MISMATCH RESPONSES: A DCM/MEG STUDY

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Attention and expectation have similar behavioural effects, both enhancing detection and facilitating recognition of stimuli. However, they have opposing effects on early evoked neural activity: attention typically enhances event-related responses, while expectation reduces them. This opposition has been reconciled in the predictive coding framework, where prediction errors (lower for expected stimuli) are weighted by precision associated with attentional modulation. The aim of this study was to corroborate the predictive coding account of attention and expectation based on MEG data and modelling. Attention and expectation were orthogonally manipulated in an auditory mismatch paradigm. Brief tones (sine waves at 6 possible frequencies) were presented in a roving oddball sequence over the course of multiple trials. In a given trial, the tones could be played at two latencies with 50% probability for each latency. Participants (N=20) attended to one of the latencies (randomised across blocks) and were instructed to detect tone omissions. As hypothesised, analysis of evoked responses revealed that expectation and attention had opposing effects on ERFs. Crucially, mismatch negativity (response to deviants vs. standards, reflecting a violation of sensory expectation) was enhanced by temporal attention at 190-210ms post-stimulus over frontocentral channels, speaking against its supposedly pre-attentive nature. The differential effects of attention and expectation were modelled in a canonical microcircuit using dynamic causal modelling of evoked responses, comparing models that allowed for extrinsic vs. intrinsic connectivity modulations at different levels of processing hierarchy from sensory to frontal areas. The modelling results cast mismatch negativity in terms of the recursive interplay of sensory predictions and prediction errors. On the other hand, temporal attention was linked to the gain of superficial pyramidal cells, extending previous empirical and modelling work on the role of precision of prediction errors in perceptual processing.

P3-034

DESPIKIFICATION OF MEG AND SEEG SIGNAL FOR INVESTIGATING EPILEPTIC OSCILLATIONS IN THE GAMMA BAND

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Introduction: Oscillations in the gamma band has been intensely investigated both in cognition and on epileptic discharges. One difficulty in the characterization of such oscillations in epilepsy is that they are often mixed with epileptic spikes, which have power across a large range of frequencies, including the gamma band. In cases when spikes and oscillations overlap in the time-frequency plane, separation of the two may prove difficult. We propose here to use a strategy developed in EEG-fMRI for removing pulse-related artefacts and to 'despikify' the MEG and EEG traces, and as a consequence better characterize the underlying oscillations.

Methods: The algorithm consists in performing on each channel an SVD on the matrix formed by stacking spikes, as proposed by (Niazy et al 2005). Wavelet denoising can be applied when necessary for removing residual oscillations on the SVD temporal bases. Then the data is projected on these bases, and the resulting model is subtracted from the data. We first tested the method on simulated data, consisting in a mixture of spikes mixed and oscillations in the gamma band with different level of overlap. We then applied the method on SEEG data (preictal phase) and MEG data (interictal phase, after ICA decomposition).

Results: We observed that for simulated data despikification lead to a good separation which was confirmed by a time-frequency domain, even for a high level of overlap between spike and oscillation. For SEEG the despikification revealed strong pre-ictal oscillations. For MEG data, despikification seems promising as a pre-processing step before source localization.

Conclusion: Despikification is a new strategy that could help investigating high frequency oscillations in the gama band, even in the presence of cooccurring spikes.

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P3-035

MOVEMENT-RELATED EVOKED FIELDS USING TRIGGERS FROM ACCELEROMETER SIGNALS

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Objective: To describe a reliable method to map human primary sensorimotor (SM1) cortex using averaged magnetoencephalographic (MEG) signals related to continuous voluntary finger movements monitored with an accelerometer.

Methods: Three healthy subjects performed rhythmic, self-paced (at about 3 Hz) right-index finger flexion-extension movements for 3 minutes. The movements were monitored with a three-axis accelerometer (ADXL335). One hundred movement-related evoked fields (MREFs), from -1000 ms to 200 ms, were averaged with respect to the peak of the Euclidian norm of the three orthogonal accelerometer signals, i.e., finger deaccelerations due to the finger touching the table. Sampling rate of 1000 Hz and band-pass filter (0.03–330 Hz) was used. The corresponding neuronal source was modeled using equivalent current dipole (ECD) in a spherical head model, and superimposed to the coregistrated magnetic resonance images.

Results: MREFs showed clear peaks around 100 ms after the peak acceleration at the right rolandic MEG sensors contralateral to the finger movement. The corresponding sources were located in the hand area of the left SM1 cortex. No significant magnetic artifacts in MEG signals were noted related to the finger movements.

Conclusion: MREFs triggered using finger acceleration is a simple and reliable method for human sensorimotor mapping.

P3-036
DIFFUSION MAGNETIC RESONANCE INFORMATION AS A REGULARIZATION TERM FOR MEG/EEG INVERSE PROBLEM

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There are several regularization terms that are used to constrain the Magnetoencephalography (MEG) and the Electroencephalography (EEG) inverse problem. These imaging modalities are characterized by their high temporal and low spatial resolution, so the question of adding information from a high spatial resolution imaging modality is admissible. It has been shown that the brain can be divided into several regions[1] with functional homogeneity inside each one of them. To locate these regions, we use the structural information coming from the diffusion Magnetic Resonance (dMRI) modality.

To investigate the importance of the dMRI information in the MEG/EEG inverse problem, we compare the source intensities obtained by constraining the inverse problem with the dMRI parcellation to the ones of the random clustering and some other well used approaches with the use of synthetic and real[2] MEG/EEG data. The two parcel-based inverse problem [3] add regularization terms, that consider the parcel information, to the minimum norm approach. The first approach assumes a constant intensity for each parcel while the second allows some variations that depends on the size of the parcels. The stability of the solutions to the number of parcels and noise are also covered in this work.

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P3-037
ALPHA TO GAMA CROSS FREQUENCY COUPLING IS ABNORMAL IN AUTISM SPECTRUM DISORDER

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Phase amplitude coupling (PAC) describes the linking of the phase of a low frequency oscillation to the amplitude of a high frequency oscillation. Prior adult studies have shown that a basic property of resting-state brain activity is the PAC of posterior alpha oscillations to posterior gamma oscillations. Given reports of abnormal parietal-occipital resting state alpha power in children with autism spectrum disorder (ASD), the present study examined whether resting-state alpha-to-gamma PAC is altered in ASD. Simulations were first performed to evaluate the performance of traditional PAC analyses and optimize the PAC computation. In particular, to avoid false-positive PAC findings, simulations showed the need to use a restricted passband to filter the upper frequency band and the need for longer epochs of data. The simulation results were used to optimize methodology in the population study. For the human study, eyes-closed resting-state magnetoencephalography data were acquired from 26 children with ASD and 22 typically developing (TD) children. Source modeling provided continuous time course data at a midline parietal-occipital source for PAC analyses. Greater alpha-to-gamma PAC was observed in ASD than TD ($p<0.02$). In both groups gamma activity increased at the alpha phase associated with the peak of the alpha oscillation. This similarity in PAC dynamics indicates a commonality in the PAC mechanism across groups. In addition, an association between alpha power and alpha-to-gamma PAC was observed in both groups, although this relationship was stronger in ASD than TD ($p <0.05$). Present results demonstrated that although alpha-to-gamma PAC is present in children, this basic resting-state process is abnormal in children with ASD. In summary, simulations and the human data highlighted the need to consider the interplay between alpha power, epoch length, and choice of signal processing methods on PAC estimates.

P3-038
ASSESSING THE DYNAMICS OF BRAIN CONNECTIVITY: NETWORK CHANGES RESULTING FROM LEARNING REVEALED USING GRAPH THEORY

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Characteristics of brain networks derived using functional connectivity (FC) analysis can be quantified using graph theory. Quantifying network characteristics is important as it may permit comparison of networks derived from different conditions, providing insight into the dynamics of brain connectivity. In the present study we investigated the ability of graph theory to capture changes in network characteristics. We utilized a motor learning paradigm in which behavioural change is observed within a single experimental session, and changes in brain activity are expected to underlie the observed behavioural changes.

Eighteen non-disabled subjects (25 ± 4.5 years) performed a skilled unilateral visuomotor task while magnetoencephalography data was collected. Learning was assessed by comparing behavioural measures (accuracy and error magnitude) pre- and post-training. Coherence-based FC between eighty cortical nodes was calculated pre- and post-training and compared to a resting condition to reveal two task-positive networks. Characteristics of the pre- and post-training networks were quantified using graph theory metrics including node degree and characteristic path length. Comparison of the pre- and post-training network metrics was performed to determine changes in brain connectivity associated with learning.

Behavioral results showed an improvement in performance based on increased accuracy and decreased error magnitude from pre- to post-training ($p < 0.05$). Underlying these behavioral changes were differences in FC between networks. Specifically, node degree for brain regions involved in early learning decreased from pre- to post-training. Node degree increased in regions known to be active in the 'learned' state. Importantly, the characteristic path length decreased post-training, indicating a more efficient network.

Results indicate that graph theory metrics can detect differences in brain networks derived from different, albeit related conditions. The ability to compare networks using graph theory has widespread applications, including investigating FC in patients with neurological disorders and assessing changes in FC resulting from interventions used in rehabilitation.

P3-039

PERFORMING NETWORK CONNECTIVITY ANALYSES BETWEEN REGIONS OF INTEREST USING MAGNETOENCEPHALOGRAPHY

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We present a method for the discovery of networked neural behaviour between many correlated regions of interest (ROIs) in the human brain, using neural activities measured with magnetoencephalography (MEG). The existence of functional networks of activity in the brain, detectable with functional imaging even during resting state measurements, is now a robust result in both the MEG and functional magnetic resonance imaging (fMRI) literature. Analyses of the connectivity between networks, or within network nodes, are common in fMRI, including many powerful methods which employ linear correlation measures. These analyses are limited in MEG by the need to remove the spurious correlations introduced across the brain by source reconstruction methods.

Existing approaches for handling the artificial correlations can be applied only in a pair-wise fashion across source dipoles (Brookes et al., 2012; Hipp et al., 2012). Here we propose a novel approach for removing spurious correlations across multiple dipoles or ROIs in the brain, in preparation for multivariate analyses such as partial correlation. We form a single time-course to represent each ROI, then remove spurious correlations using a symmetric orthogonalisation approach. We show that analysing the partial correlation of the band-limited power envelopes of the corrected ROI time-courses is a powerful technique for revealing undirected connections between regions.

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P3-040

ENHANCED CAUSALITY ANALYSIS IN SOURCE SPACE BASED ON CROSS TRIAL PHASE STATISTICS

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Magnetoencephalography (MEG) is extensively used for the investigation of oscillatory activity across brain areas. For understanding the information flow, Granger causality is used and reported to allow disclosing the brain communication pathways. Given the noisy nature of MEG, a difficulty resides in identifying the interactions related to causal relationships from those based on noise influence. The reliability is degraded in the presence of environmental and electronic noise. Biological artifacts introduce spurious brain sources after source localization. Even if causality is applied on reconstructed source time courses from "clean" MEG data, multiple and nearby sources may result in fictitious causal density.To provide non-ambiguous causality measures at the source level, we here present an approach combining:

- signal component selection using cross-trial phase statistics (CTPS)
- causality analysis using partial Granger causality (PGC)
- CTPS has been introduced to extract phase-locked activity from decomposed MEG signals. The CTPS method was originally introduced for the identification of cardiac activity. Here, the same strategy was used for the identification of activity phase-locked to an event of interest. CTPS is capable to identify strong and weak stereotypic activity in phase space from unaveraged MEG signals. When extracting components with phase-locked activity only, the SNR of the unaveraged MEG data was greatly enhanced. We investigated the effect of CTPS on the results of causality analysis on a MEG dataset obtained in response to targets in an attention orienting paradigm.We selected time courses from regions of interests representing sources with phase-locked activity prior to the causality analysis. As we assumed that this network may not be complete, we used PGC which is considered to be more robust to the effects of "hidden" sources bearing significant causal relations. The results are discussed, investigating the performance of causality analysis when focusing on phase-locked activity.

P3-041

PROPAGATION OF EPILEPTIC SPIKES REVEALED BY DIFFUSION-BASED CONSTRAINED MEG SOURCE RECONSTRUCTION

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Magnetoencephalography (MEG) source reconstruction is becoming recognized as a useful technique to non-invasively localize epileptic foci. Giving a direct access to the temporal succession of cognitive processes,

this modality should allow us to follow in source space the propagation of spikes. Unfortunately, the inverse problem being sensitive to the functional noise of MEG recordings, the recovery of dipoles magnitude is usually performed on averaged trials. However, averaging epileptic spikes is difficult (different types, different propagations [1]), thus studies which average epileptic spikes at the maximum of their intensity can not explore the propagation characterizing each epileptic spike.

This abstract presents a methodology to study the propagation of epileptic spikes from MEG data. The main ingredient of the approach is a minimum norm reconstruction constrained to give a constant solution in cortical parcels obtained from diffusion MR images [2]. Parcels are defined as areas with similar structural connectivity [3].

This method gives focal reconstructions and is very robust to functional noise. Thus, the MEG inverse problem can be applied to a single spike. Furthermore, the reduction of dimensionality of the source space (induced by parcels) allows us to extract compact information about the spatial and temporal propagation of the spike. The reconstruction method is completed with a method which allows us to follow the time-dependant activity of the diffusion-based areas and identify the areas at the origin of the activity.

The method has been applied on three different spikes of a single subject revealing various paths of propagation.

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P3-042

WEDGE MUSIC: A NOVEL APPROACH TO EXAMINE EXPERIMENTAL DIFFERENCES OF BRAIN SOURCE CONNECTIVITY PATTERNS FROM EEG/MEG DATA ROBUST TO VOLUME CONDUCTION

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Synchronous oscillatory activity of different brain regions has been shown to form a neural basis of different cognitive functions and processes. Although being the only non-invasive measurement techniques providing sufficiently high temporal resolution, it is difficult to study these interactions from electrophysiological scalp recordings such as EEG and MEG. First, the estimation of neuronal sources is not uniquely solvable. Second, observed synchronization between sensors does reveal little about underlying brain sources and can as well arise from independent neuronal sources. Here, we introduce a novel method to estimate synchronized, i.e. interacting brain sources at a specific frequency or band. The data driven calculation is solely based on a low dimensional approximation of the imaginary part of the cross-spectrum as opposed to the imaginary part of coherency as the normalization for the latter includes dependencies on non-interacting sources. This construction a) serves as a trustworthy quantity robust to the problem of volume conduction and b) reduces dimensionality for solving the inverse problem. Generally speaking, the method quantifies how strong a synchronization between a distinct pair of brain sources is represented in the data. Principally, all pairs of pre-defined locations inside the brain can be used as an input which is computationally exhaustive. In contrast to that, one can employ reference sources that have been identified by any prior source reconstruction technique. We introduce different variants of the method and evaluate the performance in simulations. As particular advantage, Wedge Music is capable of investigating differences in brain source interactions between experimental conditions. We exemplarily show the application on MEG resting state data and find locally synchronized sources in the motor-cortex based on the sensory motor idle rhythms. Furthermore, we contrast hand and foot movement in EEG motor imagery data where we also find local interactions in the expected brain areas.

P3-043

GROUP-WISE ICA FOLLOWED BY BEAMFORMING ALLOWS ROBUST NETWORK DETECTION FOR FUNCTIONAL CONNECTIVITY ANALYSIS IN MEG

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Beamformers are popular inverse models for source reconstruction in MEG. These algorithms rely on a minimization of total power while constraining gain in voxels of interest. However, in cases where several strong sources are present in the data, beamformers are susceptible to errors in resolving these sources due to spatial leakage. As many empirical studies try to determine functional coupling among brain regions, source reconstruction is merely a precursor to assessing these relationships. Here, we developed a method that used group-wise independent component analysis (ICA) to decompose sensor signals into maximally independent time courses. The end goal was to determine functional connectivity changes within alpha/theta frequency bands using phase lag index (synchronization measure) during a learning task. First, we modeled the data's intrinsic dimensionality with Bayesian Information Criterion and reduced data dimensions with principal component analysis. Then, we performed a single decomposition and projected group-based weights onto individual participant data. The data underwent two separate analyses from this point. We applied beamforming to obtain spatial locations of the components (32 in total). The functional images were transformed to MNI space and group averages were computed. The location within a spatial cluster that had the highest pseudo-z statistic (measure of neural activity normalized by noise) was considered the region that corresponded to the scalp distribution of that component. A large proportion of components were localized to single regions while a few

consisted of 2-3 regions. Second, we took the individual component time series and calculated phase differences for all component pairs. The results showed that neuronal coupling in alpha and theta bands was indicative of separate stages of learning. We suggest that extracting sources/networks in a data-driven pipeline that uses group-wise ICA holds value for identifying whole-brain changes in functional connectivity that can subsequently be related to behavior.

P3-044

UTILISING DYNAMIC CAUSAL MODELS TO EXPLORE NEURONAL NETWORK DYNAMICS OF GENETIC ION CHANNELOPATHIES

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Genetic channelopathies represent a newly-discovered class of neurological disorders where ion channel-coding gene mutations lead to varied disease states, including epilepsy, migraine, neuromuscular disorders, and ataxias. These channel mutations occur throughout the body as well as in the central nervous system. Dynamic Causal Modelling (DCM) is a model-based analysis framework designed to study synaptic mechanisms underlying brain dynamics. The models include representations of pre and post-synaptic cell activity with specified dynamic parameters that represent different ion channel species. Hence, channelopathies represent a uniquely specific population from which validation of this modelling analysis can be obtained. In order to test this non-invasive assay of neuronal ion channels, we extended a conductance-based neural mass model of interacting cortical regions. The model includes direct neurotransmitter-mediated sodium, calcium, and chloride responses to glutamate and GABA, in addition to indirect potassium channels which respond to ongoing membrane potential fluctuations. The updated model includes a parameter for inward-rectifying potassium channels. Using this updated model, we fit DCMs to 92 healthy control participants' magnetoencephalographic ERPs during an auditory mismatch negativity paradigm. We also fit DCMs to two patients with genetic channelopathies. Patient 1 had an inward-rectifying potassium channel gene mutation, while patient 2 a voltage-dependent presynaptic calcium channel gene mutation. As expected, when comparing ion channel parameters between patients and controls, both patients showed channel-mediated effects. Patient 1 showed a significant difference in their potassium leak conductance compared with controls, while patient 2 showed a significant difference in their sodium, calcium, and chloride neurotransmitter-mediated dynamics. Using a leave-one-out technique, we found no significant differences between normal participants on ion channel-mediated dynamics. These findings suggest that DCM is a powerful technique that can be used to explore specific ion channel-mediated dynamics on cortical network connectivity.

P3-045

GPS: A GUI-BASED AUTOMATED PROCESSING STREAM FOR KALMAN-FILTER ENABLED GRANGER ANALYSIS OF MR-CONSTRAINED MEG/EEG DATA

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The Granger Processing Stream (GPS) is a freely distributed tool for performing Granger causality analysis of MR-constrained MEG/EEG data (https://www.martinos.org/software/gps). Using a graphic user interface, GPS acts as a front end interface to automate MR anatomical reconstruction using Freesurfer, and source space minimum norm estimates of individual and group averaged brain activation based on MEG/EEG using MNE. Regions of interest (ROIs) are created algorithmically by identifying highly active vertices, and then comparing their normalized activation functions to first eliminate redundant vertices as required by Granger analysis, and then to identify regions around activation centroids that show homogenous activation functions to characterize the spatial extent of each ROI. Granger causality is calculated using time-varying VAR models created using a Kalman filter technique. This approach has several advantages including obviating the need for unrealistic assumptions about stationarity, addressing the inherent noisiness of MEG/EEG measures, and making it possible to quantify the strength of partial Granger causation (Granger Causation Index) independently at each timepoint over networks that frequently consist of 20-40 ROIs. GPS uses a bootstrapping method to generate independent null distributions of GCi values at each timepoint for all directed connections for the purposes of significance testing. The strength of GCi for the same connection in two experimental conditions is tested using a binomial technique. GPS visualizes the results of analyses in the form of several types of GCi timeseries graphs, and graphs showing directed connectivity, and ingoing/outgoing hub structure over cortical surfaces or circle graphs. GPS also automatically manages file structure.

P3-046

CRITICAL-STATE DYNAMICS OF SPONTANEOUS OSCILLATIONS LEADS TO OPTIMAL RANGE OF EVOKED RESPONSES

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Critical dynamics have been observed in neural networks at different levels of organization, where activity tends towards the balance between order and disorder. Different computational models have been created that each exhibit some aspect of this critical behavior, which in turn were associated with optimal information processing such as memory storage or response to stimuli. Using threshold stimulus detection tasks in humans it has been shown that ongoing oscillations alter the likelihood of stimulus detection,

with certain amplitudes or phases of an oscillation having a higher likelihood of detection. The ongoing oscillations themselves are affected when a stimulus is detected.

To investigate the relationship between critical-state dynamics and oscillations in the processing of stimuli, we used a previously developed neuronal network model that exhibits neuronal avalanches on short timescales and long-range temporal correlations of oscillations on long timescales. By altering the excitatory/inhibitory connectivity balance, networks with sub-, critical and super-critical dynamics were created. These networks were probed with varying intensities of stimulation, and their responses analyzed in terms of the dynamic range of post-stimulus phase locking and how post-stimulus effects were modulated by the amplitude of pre-stimulus oscillations.

Our results indicate that networks with critical oscillatory dynamics show the largest dynamic range of post-stimulus phase locking, that this effect is significant for more than 250 ms and, interestingly, that only critical networks exhibit pre-stimulus amplitude dependence of post-stimulus phase locking. These results show that critical networks go through periods of being more or less sensitive to stimuli based on their ongoing activity, which could be important for attentional mechanisms. These results also imply that "the critical state" is not merely one state from a functional point of view and loss of LRTC should lead to impairments in stimulus processing.

P3-047

NARRATIVES CONSISTENTLY MODULATE ALPHA-BAND ACTIVITY

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The analysis of inter-subject correlations (ISC) allows one to study neural processing of natural stimuli (Hasson et al., 2004). Dmochowski et al.(2012) analyzed event-related (ERP) activity in electroencephalographic (EEG) signals during movie viewing, while Honey at al. (2012) analyzed amplitude modulations of brain oscillations using electrocorticography (ECoG). Here we investigate whether ISC of amplitudes of brain rhythms can also be observed in the alpha-band (8-12 Hz) of the EEG. In order to extract alpha oscillations with consistent amplitude modulations, we employ canonical source power correlation analysis (cSPoC, Dähne et al., 2014). We analyze 32-channel EEG data of N=30 subjects who watched a scene from a movie and listened to an excerpt from a stand-up comedy twice. After artifact removal, the data were filtered in the alpha range using complex Morlet wavelets. Then we applied cSPoC to project all of the 30 datasets jointly onto five latent components. The analysis yielded components with spatially smooth predominantly occipital and left central spatial topographies. For both stimuli and viewings, the first alpha component resembled the first component obtained in Dmochowski et al., and may therefore comprise fast constituents of the same ERP. The level of ISC of alpha band-amplitudes ($0.01 < r < 0.04$, $p < 0.05$) was comparable to the level achieved for evoked responses (Dmochowski et al.), but below the level reported in Honey at al. for ECoG data. Grand-average alpha-band amplitudes of cSPoC components, however, showed a high degree of similarity ($0.13 < r < 0.41$, $p < 0.05$) between viewings. Summarizing, we revealed that narratives presented as audio-visual or auditory stimuli modulate alpha band components with a time course that is consistent across subjects and across repeated presentations.

P3-048

INTRODUCING SPOC: A MULTIVARIATE ANALYSIS FRAMEWORK FOR THE INVESTIGATION OF CROSS-FREQUENCY POWER COUPLING AS WELL AS FOR MULTIMODAL INTEGRATION OF EEG/MEG POWER WITH HEMODYNAMICS

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We present the SPoC (Source Power Comodulation) framework for source separation of multivariate EEG/MEG/LFP recordings, which focuses particularly on envelope/power dynamics of oscillatory sources. In the SPoC framework, the source separation is based directly on the quantity of interest (co-modulation of power dynamics), rather than on auxiliary assumptions (e.g. mutual independence).

The SPoC family of algorithms optimizes spatial filters such that the envelope/power of extracted EEG/MEG activity maximally correlates with:

- a univariate signal such as a behavioral- or stimulus variable (RT, ratings, intensity, etc.) (SPoC, Dähne et al. 2014a)
- a signal which is simultaneously extracted from a multivariate input such as concurrent hemodynamic measurements (e.g. NIRS, fMRI) (mSPoC, Dähne et al. 2013)
- the envelope of simultaneously extracted oscillatory source signals within or across frequency bands and within or across multiple subjects (cSPoC, Dähne et al. 2014b, under review)

The SPoC algorithms are benchmarked in extensive simulations as well as on real-world data against state-of-the-art analysis techniques such as Independent Component Analysis (ICA) and Canonical Correlation Analysis (CCA).

In a study on loudness-modulated steady-state auditory evoked potentials (SSAEP), SPoC achieves statically significantly larger correlation between stimulus intensity (loudness) and power at the SSAEP frequency than ICA or Regression (Dähne et al. 2014a). mSPoC outperformes CCA in the task of integrating concurrently measured EEG and NIRS (Dähne et al. 2013). cSPoC extracts maximally envelope correlated alpha and beta sources on resting state data in an unsupervised manner (Dähne et al. 2014b, under review).

The SPoC algorithms extract brain oscillations, the power dynamics of which co-modulate with parameters of interest. Thus, the framework will be a valuable tool in the quest for understanding the role of neural oscillations within and between subjects.

P3-049

COMPARISON BETWEEN BEAMFORMING AND MINIMUM-NORM ESTIMATES FOR THE DETECTION OF LONG-RANGE COHERENCE IN MEG SOURCE-SPACE

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A critical aspect of source-level connectivity with magnetoencephalography (MEG) is the possible influence of the chosen inverse method on the reliability of subsequent coupling analysis. The time series of the cortical sources can be reconstructed using various MEG inverse methods, but whether and how each one differentially affects source coupling measures is still poorly understood. Here, we address this question by investigating the impact of different source estimation methods on source connectivity detection. To this end, we simulated thousands of coupled source configurations and computed the MEG field they generate at the sensor level. In particular, we created alpha-range oscillatory coupling between the time series in each source and varied numerous parameters including: coherence amplitude, source size (point-like sources to extended patches of cortical activity), signal-to-noise ratio (SNR) and randomly varied the source locations. We then evaluated the power and coherence maps obtained using L2-Minimum-Norm estimate (MNE), Linearly Constrained Minimum Variance (LCMV) Beamforming, and Dynamic Imaging of Coherent Sources (DICS). To assess and compare the performance of the various methods in terms of power and coherence estimation, we computed receiver operating characteristic (ROC) curves and the area under the curve (AUC). These extensive simulations provided critical insights into the strengths and limitations of the three investigated methods. The ROC analysis also provides insights into the effects of regularization, SNR, coupling strength and patch size on the results. Our results also triggered further investigations into possible limitations that the various methods may face when the elemental dipoles within the cortical patches are highly coherent and we also explored the role of source orientation constraints. Taken together, our results highlight the strengths and specific shortcomings of beamformer and minimum-norm methods with regards to connectivity estimations in source space.

P3-050

SPECTRAL SIGNATURES OF BRAIN NETWORK DEVELOPMENT

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Introduction: Understanding the intricate connectivity changes in brain networks that occur over the lifespan will not only help to define what constitutes normal brain development and aging, but also provide benchmarks against which to assess what goes awry in developmental and psychiatric disorders. Existing knowledge on the development of brain networks is based on fMRI studies that demonstrate that brain networks show a higher level of local processing in children. With maturity, the processing shifts into a globally distributed network. However, since fMRI is an indirect correlate of neural activity, here we have investigated whether physiologically relevant oscillations measured directly with MEG, contribute to brain network development.

Materials & Methods: We used network analysis in resting state MEG data from 71 healthy subjects divided in to three groups (8-12 years, n=23; 13-17 years, n=19; 18-47 years, n=29) to investigate how oscillations in different frequency bands contribute to developmental changes in brain networks. Connectivity was measured between 450 cortical regions by measuring temporal correlation in amplitude of MEG signals and analyzed with network theory and Graph Analysis.

Results: At the group mean level, the spatial pattern of intrinsic connections were markedly different for different frequency bands. Developmentally, our grouping showed an age related decrease in efficiency of local networks connected by gamma ($F=8.44$, $p=0.001$), alpha ($F=3.9$, $p=0.026$), delta ($F=9.6$, $p<0.0001$) and theta bands ($F=6.7$, $p<0.0001$). In contrast, efficiency of globally distributed brain networks increased for gamma ($F=4.25$,$p=0.02$) and delta ($F=5.7$,$p=0.05$) bands (Effect: $F=7.1$, $p<0.0001$;network density=5%). (Fig-1)

Discussion: This is the first evidence to show that specific neuronal frequencies mediate developmental changes in brain networks from local to a global topology. These findings have significant implications for characterizing the normative range for brain network maturation. These benchmarks will have utility in early detection of neurodevelopmental disorders like Autism and ADHD.

P3-051

CONNECTIVITY ANALYSIS USING VIRTUAL TANGENTIAL COMPONENTS OF THE NEUROMAGNETIC FIELDS

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Magnetoencephalography[MEG], as a non-invasive tool to measure brain activities with high temporal resolution, is getting increasing attention in the area of neurosciences and clinical applications. With growing interest to understand functional connectivity during rest and task conditions, various approaches have been introduced to estimate the coherence between brain signals in both sensor and source space. Interpretations of the connectivity results, however, can be difficult, especially in sensor level analysis, due to the effects of field spread. Here we present a method to circumvent the field spread issue in sensor connectivity analysis. In summary, the MEG data recorded with axial gradiometers are transformed to virtual data at standard grid points with tangential magnetometer configuration, based on a minimum-norm estimate. The imaginary part of the coherency between sensor pairs is then calculated using the virtual data, to estimate connectivity

between scalp brain areas. The validity of this new method is tested using computer simulation data first. The results with real MEG data are demonstrated, by comparing multiple metrics including the phase-locking-value, the magnitude squared coherence and the imaginary part of coherency, calculated from the same data set.

P3-052
CONNECTIVITY PATTERNS OF SLEEP MICROSTRUCTURAL ELEMENTS

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During Non-Rapid Eye Movement (NREM) sleep brain is considered to be relatively disconnected from the environment, while connectedness between brain areas has also been found decreased. Evidence indicates that these changes are fast and dynamic allowing short periods for evaluation of environmental stimuli followed by sleep promoting procedures. Aiming to an understanding of the role played in the above by specific elements of sleep microstructure, we developed a tool with millisecond time resolution appropriate for assessing and presenting brain connectivity during NREM sleep spindles. It is based on the observation by Nolte (2004) that when the phase between two signals is zero, the coherence value can be attributed to volume conduction rather than functional neuronal connection. Excluding this value we developed the (non zero) NZ-coherence. The new tool counts among the effective connectivity tools as advantageous in (a) its superb time resolution (b) ability to study events clustered from different time periods or subjects (c) simultaneous study of any choice from all possible combinations of EEG electrodes and display their NZ-coherence in time-frequency topological maps and (d) parameterization of all the plots included in the maps regarding frequency, time and NZ-coherence threshold. Preliminary results from 360 fast spindles recorded in whole night sleep of two young adult healthy volunteers the use of NZ-coherence indicated a prevailing connectivity pattern of causal interactions mostly from centroparietal regions (C3, Cz, C4, Pz, P3, P4) to right frontotemporal regions (F8, T4). The study aims to help our understanding of the role played by spindles not only in sleep maintenance but also in memory consolidation and in several neuropsychiatric disorders.

P3-053
CONNECTIVITY IN LANGUAGE NETWORK AFTER HEMISPHEROTOMY

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Hemispherotomy is a surgery isolating a diseased hemisphere, leaving an intact hemisphere connected to the rest of the brain. Now that epilepsy is more and more understood as an abnormal network, we could expect a large scale network change after hemispherotomy. Despite that cognitive function including language often improves following hemispherotomy, there have been few studies addressing how this improvement happens. Here we aimed to explain improved language function in a patient after the right-side hemispherotomy through comparing the connectivity pattern in the language network before and after hemispherotomy using a magnetoencephalography (MEG) and diffusion tensor imaging (DTI). Overall connectivity increase in the language network measured by a partial directed coherence was obvious after the operation both in the performing and the resting brain. Post-operatively, connectivity strength was strikingly increased at the junction area of the parietal and the temporal lobes and in the inferior frontal gyrus, which have been known as powerful auditory-motor interfaces integrating language-motor information. It is particularly noteworthy that the changed language network resembled the healthy network more than before. This was also supported by the anatomical connectivity reflected in the increased fractional anisotropy in the areas aforementioned. Collectively, we propose that network integrity, both functional and anatomical, contributes to the improvement of language function in our patient. We might expect that the enhanced function was concomitant with the increased connectivity in the language network and with the sharing of more key features with the healthy language network, presumably due to the restored language network, free from the intervention of the epileptiform discharges. This finding provides a unique evidence of unilateral hemispheric reorganisation enabling an effective use of the network due to a beneficial surgery, hemispherotomy.

P3-054
DYNAMIC CAUSAL MODELING (DCM) OF SEMANTIC AND EPISODIC MEMORY IN HEALTHY ELDERLY SUBJECTS: AN MEG STUDY

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This study aimed at investigating the neural correlates of semantic and episodic memory in healthy elderly subjects using a DCM approach with Magnetoencephalography (MEG).

Thirteen subjects (age: 62.8+/-0.8years) were recorded on a whole-head 151-channels CTF MEG system in a semantic task (encoding phase of famous and unknown faces) paired with an episodic task (recognition phase

of old – previously seen – and new faces) (see La Corte et al., 2012 for details). Event-related fields (ERFs) in response to the faces were computed for each face type in each task. Using SPM12b, we then performed source reconstruction, including deep hippocampus structure, in consecutive time windows (0-200/200-400/400-600/600-800ms). We identified 9 regions of interest that were activated during the semantic and episodic tasks. DCMs were constructed using those 9 ROIs as follows: a single input in the visual cortex, bi-lateral sources in the fusiform gyrus (Fg), parietal (Pa) and frontal (Fr) cortices, and hippocampus (Hip). Fourty-three anatomically plausible models were tested by varying the bilateral connections between the 9 ROIs. We used standard DCM for MEG routines to estimate each model separately in each task and each subject. Bayesian model selection (BMS) and Bayesian model averaging (BMA) were used to compare the evidences of the models.

We found that models including connections between Fg and Fr, Pa and Hip, Fg and Pa respectively were more plausible than models without these connections. Moreover, using these winning model families, we showed statistical differences in connectivity modulation between the tasks: there was a stronger modulation of the Fr to Fg connection in the semantic relative to the episodic task in the left hemisphere, while the opposite was true in the right hemisphere. These results underline the involvement of this connection during semantic and episodic retrieval of faces over left and right hemispheres, confirming the lateralisation of memory processes.

P3-055

TIME-VARYING CONNECTIVITY ANALYSIS BASED ON MEG BRAIN IMAGING

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Nowadays, importance of measuring connectivity between spatially separate, but functionally related brain regions has become of key interest in the study of human neural functions. Consequently, Magneto/Electro-encephalographic (M/EEG) data give a direct non-invasive measurement of neural brain activity that offer connectivity information among brain regions. Functional connectivity analysis based on M/EEG brain images usually comprises two stages: First, the M/EEG signals are mapped into the source space using an inversion method (MSP, LORETA, etc.); then, connectivity analysis is performed using predefined regions of interest. Nevertheless, the common assumption about M/EEG stationarity (time-invariant process) is a strong limitation for understanding real behavior of underlying neural networks. Here, we propose an approach for finding networks between brain regions, connected by functional associations (functional connectivity) that vary along time. To this end, we compute a set of a priori spatial dictionaries that represent brain regions with similar temporal stochastic dynamics. Then, we model the relationship between the selected regions as a time-varying process. We tested our approach in both simulated and real EEG data. Results show that inherent interpretability provided by the time-varying process can be useful to describe underlying neural networks.

P3-056

INTERACTION SPACE RAP-MUSIC FOR ESTIMATION OF TRANSIENT NETWORKS FROM MEG DATA

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MEG reflects electrical activity of neuronal assemblies that coalesce and decoalesce in time providing for massively parallel and dynamic flow of information exchange in the brain. There is a growing evidence that our behavior is mediated by simultaneous activity of several interacting and simultaneously active cortical networks. Not only the location of network nodes but also the temporal profiles of such interactions are of interest. The existing methods are primarily concerned with proposing novel measures of synchrony to be applied to the cortical region activity signals extracted from the MEG data using beamforming or other spatial filtering approaches.

In this work we propose to render the task of estimating network topology and temporal profiles as a source estimation problem but in the space of interacting topographies. The proposed point of view has a number of benefits as it allows to use the wealth of techniques and intuition accumulated in the community when dealing with source estimation problems. Operating in the interacting topographies space we use subspace matching metrics to extract a set of networks with their synchronicity profiles that explain the variance in the imaginary part of sensor space coherence, much like regular dipoles and their activations explain the variance in the regular evoked responses.

The preliminary results of application of this method to a simple language paradigm comparing verb and noun forms of motor action related words allowed to observe functional coupling between Broca, Wernicke and sensorimotor cortex and recover temporal profiles of coupling strength evolution. The observed synchrony patterns are in agreement with the current prevailing hypothesis about distributed language comprehension mechanisms stipulating the involvement of sensorimotor cortex in recognition of motor-related words.

P3-057

FREQUENCY SPECIFIC NETWORK INTEGRATION AND SEGREGATION PROPERTIES OF MEG RESTING STATE FUNCTIONAL CONNECTIVITY

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Resting state networks (RSNs) are sets of brain regions exhibiting temporally coherent activity fluctuations in the absence of imposed task. RSNs have been widely studied with functional Magnetic Resonance Imaging in the infra-slow frequency range (< 0.1 Hz) [1]. However, neuronal communication occurs at much faster frequencies (1-100 Hz) and is sustained by a mechanism of phase synchronization of neural oscillations [2].

To investigate the relationship between oscillatory coupling and RSNs phenomenology, we examined frequency specific all-to-all MEG functional connectivity (fc-MEG) by phase-shifted coherence estimated from the Multivariate Interaction Measure (MIM) [3,4] in resting-state source space signals. To assess statistical significance of MIM values a Jackknife procedure over time epochs was applied.

Results for the alpha band (Fig.1a) show that the same frequency band can serve as a substrate for long range interactions in both internal network coupling and in the integration between control and data processing networks (Fig.1b and 1c), thus supporting the hypothesis that phase coding of oscillation rather than frequency can serve for information integration at different levels. Moreover data driven strategies disclose the emergence of frequency specific network-like topographies as well as frequency specific topological properties (e.g., network centrality, node hubness), possibly speaking about differential links between anatomical and functional levels according to oscillation frequencies and relative phases.

Figure 1. (a) Average fc-MEG map in the alpha band; (b) fc-MEG map for a seed node in left posterior intra parietal sulcus (DAN) shows coupling with visual areas (VN); (c) fc-MEG map for a seed node in left medial prefrontal cortex (DMN) shows coupling with posterior parietal cortex (DMN).

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P3-058
EMPIRICAL BAYES FOR SUB-CORTICAL STRUCTURES

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There remains some controversy about the ability of MEG to detect activity in subcortical structures such as the hippocampus. While some authors present evidence for detection and differential engagement of hippocampal subregions (eg Cornwell et al., 2014), others combine MEG with subdural electrode recordings and conclude that detection at low source strengths is not possible (Mikuni et al., 1997). In this work we use an empirical Bayesian scheme in conjunction with commonly used current density priors (Minimum Norm, Beamforming and Multiple Sparse Priors) to reconstruct electrical activity simulated on the cortex or hippocampus. By comparing anatomical models with and without a hippocampal mesh we can test directly for evidence of hippocampal activity. We show the robustness of this discrimination at varying levels of simulated hippocampal current density, signal to noise ratio and co-registration error.

Cornwell BR, Overstreet C, Grillon C. Spontaneous fast gamma activity in the septal hippocampal region correlates with spatial learning in humans. Behav Brain Res. 2014;261:258-64.

Mikuni N, Nagamine T, Ikeda A, et al. Simultaneous recording of epileptiform discharges by MEG and subdural electrodes in temporal lobe epilepsy. Neuroimage. 1997;5(4 Pt 1):298-306

P3-059
ASSESSING SUBCOMPONENTS OF RESTING STATE NETWORKS AND NETWORK VISITATION WITH MEG

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Developing better methods for accurately deriving resting-state networks(RSNs) is a topic of great importance to neuroscience and by extension Psychiatry. This is especially true for magnetoencephalography (MEG) and other electrophysiological modalities, where limited spatial resolution, and inverse modelling error limit the precision with which RSNs can be derived. Existing methods for extracting RSNs from MEG data (e.g. Brookes et al., 2011) simultaneously compromise MEG's characteristic temporal resolution, which could be a key feature in determining normal and pathological resting-state networks. Jones et. al. (2010) has shown in fMRI RSNs how characteristic variations in functional connectivity can be accounted for by nonstationary visitation and dwell time in resting-state networks. Borrowing considerably from Brookes, we show two things: 1). that RSNs can be adequately derived from single subject samples with considerably better spatial precision than for concatenated data, and 2). that higher frequency sampling of the Hilbert amplitude envelope yields meaningful temporal components(sub-networks), not found in the lower frequency ranges employed previously(0.5-1Hz). In addition, we will discuss possible methods for measuring visitation of well characterized networks with MEG.

P3-060
EFFICIENT DIMENSIONALITY REDUCTION OF THE LARGE-SCALE CONNECTIVITY PROBLEM

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To identify the dynamical interactions between multiple regions of the human brain has attracted major interest in recent years. A wide variety of functional and effective connectivity models and metrics have been proposed to reveal regional neural interactions from MEG and EEG source time series. However, this is leading to a computational conundrum, because of the necessity of sampling the convoluted geometry of the brain with thousands of elementary current sources, hence yielding exponential pairwise combinations for extracting region-to-region interactions.

The restriction of connectomic analyses to a small set of predefined anatomical regions of interest is an option to keep "the curse of dimensionality" under control. However, this approach is not adequate for exploratory data

analysis. Here we propose a new data-driven selection scheme based on multi-resolution clustering indexed on the similarity of minimum-norm imaging kernel across the source support, and compare this new approach with other, more common procedures. Performance was tested on 100 scenarios based on synthetic data: we generated 10 signals using AR models in 10 random and spatially-extended locations of the brain, assigning a known pattern of connectivity including unidirectional connections (trees, chains, loops), bidirectional relationships and isolated regions. We simulated the sensor data generated by these random scouts following MEG forward modelling, with additional physiological noise. Finally, source maps were retrieved from the weighted minimum-norm estimator of Brainstorm and connectivity analysis was performed using the proposed new approach. We obtained ROC curves of sensibility and specificity for the performance of the different approaches tested, as well as a comparative estimate of the computing times required.

Our results indicate improved performances in terms of sensitivity, specificity and computational time required, and offer promising perspectives for the effective exploration of brain connectomics at the global brain scale, from time-resolved data.

P3-061

COMPARING LINEAR AND NON-LINEAR DYNAMIC FUNCTIONAL CONNECTIVITY

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Background: Recent research shows that functional connectivity in the brain is non-stationary in time, and further has significant spatial and spectral structure. Additionally, further studies have shown there are intrinsic modes of coupling in the brain based on linear (phase) relationships and non-linear (envelope) interactions. Here we measure task-driven interaction using non-linear (via. Canonical Correlation Analysis of envelopes, (CCA) [1]) and linear (via. Multivariate Coherence, (MCA) [2-3]) data in the motor cortex.

Experimental Methods: 7 participants were asked to execute a self-paced button press with the index finger of their non-dominant hand. MEG data were recorded using a 275-channel CTF MEG system at a sampling rate of 1200 Hz. Data were filtered 13-30 Hz and source reconstruction performed using a Beamformer. The left and right sensorimotor strips were isolated and multivariate leakage correction [4] applied between these regions to remove zero-phase interactions. A 3 second sliding window was then employed and dynamic changes in both linear (MCA of the raw timecourses) and non-linear (CCA of the Hilbert envelopes) connectivity assessed.

Results and Discussion: CCA shows a 12% increase (relative to baseline) in envelope correlation between the motor cortices from baseline immediately after the button press (significant to a value of $p < 0.05$). However coherence analysis highlights a 10% increase in phase synchronisation from baseline over a second later ($p < 0.001$). This delayed increase coincides with the beta-band increase in power, implying that the separate motor regions are synchronizing with each other when returning to a baseline state post task.

[1] Brookes, et al. (2014) NeuroImage 91 282-299
[2] Lyubushin (1995) Physics of the Solid Earth 34 52-58
[3] Marzetti, et al. (2013) NeuroImage 79 172-183
[4] Brookes, et al. (2012) NeuroImage 63 910-920

P3-062

CROSS-FREQUENCY INFORMATION TRANSFER DURING CONTINUOUS SPEECH PERCEPTION

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According to our previous findings [1], segmentation and coding of speech relies on a nested hierarchy of entrained cortical oscillations. Speech entrains the phase of delta and theta and the amplitude of gamma oscillations in the auditory cortex. Importantly, phase entrainment is stronger in the right auditory cortex (RAC) and amplitude entrainment is stronger in the left auditory cortex (LAC). Based on this asymmetry, we further investigated directional information transfer between auditory cortices as reference regions and all brain voxels using transfer entropy (TE).

MEG data from 22 participants was obtained during passive listening to a 7-min real-life story (story) and the same story played backward (back). To investigate the information transfer between LAC/RAC and whole brain, we first computed LCMV spatial filters from covariance matrix across the 7-min recording. Then we performed TE analysis within and between the relevant frequency bands (delta, theta, gamma) and identified information transfer that was significantly stronger in 'story' than 'back' condition (group T-statistics).

Group T-statistics revealed that the phase of speech-entrained delta and theta oscillations in RAC modulates the amplitude of theta and gamma in LAC, respectively – and more in 'story' than in 'back' condition. In addition, theta phase in LAC and RAC is top-down modulated by left frontal and motor areas more in 'story' than in 'back' condition.

Our results demonstrate that the phase of cortical oscillations is entrained by speech but also top-down modulated by frontal and motor areas in left hemisphere and more for intelligible compared to unintelligible speech. Directed interactions between entrained brain oscillations across cortical areas could be an important mechanism for the segmentation, coding and cortical analysis of continuous speech streams.

[1] Gross et al., PLoS Biol., 2013. Speech Rhythms and Multiplexed Oscillatory Sensory Coding in the Human Brain.

P3-063

REPRODUCIBILITY OF HEALTHY ADULTS' GAMMA-BAND ACTIVITY IN RESPONSE TO AUDITORY STIMULI

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Gamma-band (30-80Hz) neural activity (GAMMA) is posited to be involved in cognitive/perceptual processes. GAMMA is further hypothesized to be active in the processing of neural signals within local circuits. As such, the role of GAMMA in neuropsychiatric diseases are being increasingly investigated, though few have studied the test-retest reproducibility of GAMMA in response to auditory stimuli, which is critically necessary to interpret interval change measures (e.g. following therapy).Two paradigms tested the reproducibility of auditory GAMMA. In the first task, participants passively listened to binaurally presented 200, 300, 500 & 1000Hz sinusoidal tones (130 tones/frequency; 45dB above sensation level; 300ms duration; 10ms ramps). The second paradigm had the participants listen to a 40Hz amplitude modulated (AM) tone (1kHz carrier; 1sec duration) to elicit steady-state responses. Four participants were scanned 4 times, with 1 week between scans. A whole-cortex 275-channel MEG system (VSM MedTech) recorded the responses and the MatLab toolbox Fieldtrip was used for analysis.

Tone Analysis: Initially an atlas-defined seed region in Heschl's Gyrus was used as a target in a LCMV beamformer to derive a virtual electrode (VE). Alternate approaches included individual localization of the auditory evoked response (3-40Hz) using both a differential LCMV beamformer and standard equivalent current dipole focused on M100.

Steady-State Analysis: Atlas-based and individualized GAMMA localization were compared. Also a differential LCMV beamformer located the source of this driven gamma response at group level. From all these locations VEs were generated and aspects of the corresponding time-frequency response quantified. Reproducibility of GAMMA response was greater when the brain was driven at gamma-band frequency (representative COV=9%), though still high for tones (representative COV=33%). This compares to ~60% reduction of gamma in ASD using identical anatomical localization techniques.

P3-064

AUDITORY-DRIVEN CROSS MODAL PHASE-RESET OF CORTICAL OSCILLATIONS IN VISUAL CORTEX

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Cross modal phase-resetting (CMPR) is a candidate mechanism for multisensory integration (MSI). In principle, the dynamics of cortical oscillations following an event within one sensory modality can phase-reset oscillations in another. Romei, Gross and Thut (2012) provided evidence for both perceptual and physiological properties consistent with auditory-induced resetting in visual alpha activity. Participants were presented with brief sounds while simultaneously recording EEG. Perceptual performance was assessed via visual excitability using TMS to induce phosphenes, and EEG alpha activity assed by recording visual activity phase-locked to sound onset. Phosphene perception rate showed a periodic fluctuation at ~10 Hz, phase-reset to the auditory stimulus. These findings support the CMPR model. The current study extends this work to investigate the importance of CMPR for sensory integration at source level using MEG. First, twenty participants performed a behavioural discrimination task of apparent motion with random dot pattern that followed an auditory tone with 20 variable SOAs. It was hypothesised that perceptual performance would reveal a cyclic pattern systematically phase-locked to audition. D-prime variations with SOA showed a cyclic modulation that was explained only by fitting a 10 Hz sine consistent with an auditory phase-resetting of visual alpha oscillations. To further support the role of CMPR in modulating behavioural performance, the second experiment used MEG to probe neural oscillatory dynamics. Fourteen participants performed a unimodal detection task for auditory and visual stimuli. Using eLORETA, the underlying oscillatory components in phase-resetting were identified. This revealed a significant CMPR of auditory tones on visual alpha oscillations within a time window (50-300ms) that is consistent with the modulation in our behavioural data. In conclusion, CMPR is a candidate mechanism of MSI and seems to play a role in temporal and cross-modal sensory integration.

Romei, V., Gross, J., & Thut, G. (2012). Current Biology: CB, 22(9),807–13.

P3-066

A TIME-RESOLVED MEASURE OF CROSS-FREQUENCY PHASE-AMPLITUDE COUPLING IN NEURAL OSCILLATIONS

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Recent evidence suggests that not only examining the brain activity in each single frequency band, but also the interaction between oscillations at different frequencies can be informative in understanding the basic population mechanisms that enable brain function. This interaction, also known as cross-frequency coupling (CFC), is also thought to be a vehicle for neuronal communication, local computation, and memory processes. Thus, this concept increasingly receives interest especially in experimental cognitive neuroscience. Over the last decade, several methods have been proposed for measuring CFC intensity; however, no single method has become a true standard so far.

In the present work, we introduce a new method for cross-frequency phase-amplitude coupling estimation in spontaneous neural traces, with higher temporal resolution than existing alternatives. In the proposed method, the low frequency that modulates the amplitude of a higher oscillation is detected automatically using power spectral analysis of the high frequency envelope. The corresponding coupling strength is then measured using a mean vector length approach. Our results using synthesized data showed that this new measure is well-suited for estimating the coupling strength, and for identifying the dominant coupled frequencies, with as little as two cycles of frequency for phase oscillations.

This measure was also applied to two real datasets: first, an event-related magnetoencephalography (MEG) recording obtained from median-nerve stimulation; and second, continuous local field potential recorded from the entorhinal cortex of a rat. The analysis of dynamic phase-amplitude coupling in MEG data revealed a significant increase in CFC between alpha and gamma band oscillations, about 200 ms after stimulation in the contralateral primary somatosensory cortex. In the second dataset, a theta-gamma phase-amplitude coupling was observed in the third layer of intorhinal cortex. Interestingly, the intensity of this coupling was significantly higher in the intervals when the animal was exploring its environment, compared to resting periods.

P3-067

CHARACTERIZATION OF LOCAL AND GLOBAL SYNCHRONIZATION PATTERNS OF AUDITORY ENTRAINMENT: EXPLORING THE ROLE OF THE MODULATION FREQUENCY

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Auditory steady-state responses (ASSRs) are an evoked response recordable from the scalp when participants are stimulated rhythmically, such that the response to any one sound overlaps the responses to preceding sounds. It has been shown previously that the maximum amplitude response is evoked by sounds presented at amplitude modulation rates near 40 Hz, being thus the most widely used modulation frequency. However, previous parametric works left an important question unanswered: How do different modulation frequencies impact functional network states, from the more global (graph) level down to the individual nodes? For example, does an evoked power at 40 Hz also mean a strong long-range impact or are connections mainly confined? Or do stimulation in the alpha frequency lead to disconnections of entrained auditory cortex? In the present MEG study (N = 16) we attempt to address these questions by presenting amplitude-modulated sounds at different rates (4 - 85 Hz). Time-frequency analysis revealed increased evoked power at 40 Hz, confirming previous findings (but also at 4 and 10 Hz). Additional source analysis revealed differences in the localization of the entrained regions depending on the stimulation rate. Further analysis, applying functional connectivity combined with graph theoretical methods among these regions will explore the network level effects of auditory entrainment at different frequencies. Overall, our work combines the long established research line on ASSRs with the newer research line of “entrainment”, extending them by a network perspective.

P3-068

HARMONIC CROSS-FREQUENCY PHASE SYNCHRONIZATION IN HUMAN VISUAL WORKING MEMORY

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Visual Working memory (VWM) sustains information for further usage for a few seconds and is thought to be comprised of sensory and central executive functions. Large-scale synchronization of cortical oscillations in several frequency bands characterizes the VWM retention period. The mechanisms underlying the integration of processing distributed across frequencies into introspectively coherent VWM remain unknown.

We investigated whether cross-frequency (CF) synchronization among oscillations might serve as a mechanism for the integration of spectrally distributed processing. We recorded magneto- and electroencephalography (MEG/EEG) from 12 healthy participants during a delayed matching-to-sample VWM task. We used a data-driven analysis approach together with source reconstruction of individually optimized cortical parcellations to estimate the strength of CF-phase synchronization among cortical oscillations during the VWM retention period for frequencies from 3 to 90 Hz and for CF-ratios from 1:2 to 1:6.

We observed prominent CF-phase synchronization of θ and high-α band oscillations to β and γ-bands at ratios from 1:2 to 1:6. Importantly, we observed that β and γ oscillations were consistently CF-synchronized to high-a oscillations at harmonic ratios. On the contrary, a decrease in harmonic coupling was found for δ and low-α oscillations to β and γ-band oscillations. In addition to this harmonic CF-synchronization, we also observed subharmonic coupling from high-α and β band to lower subharmonic frequencies. Importantly, CF synchronization at harmonic ratios was correlated with accurate performance in the VWM task.

Our results show that CF phase synchrony in a complex cortical network is modulated during VWM retention and correlated with VWM load and performance.

P3-069

ALPHA BAND FUNCTIONAL CONNECTIVITY IMAGING AND PERFORMANCE OF BRAIN-MACHINE INTERFACE DURING REAL AND IMAGINED MOVEMENTS

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The brain signal recorded from the primary motor cortex (M1) is known to serve a significant role for brain-machine interfaces (BMIs) in real and imagined movements, and has also been shown to have several functional

networks with motor association areas such as the premotor cortex (PMC), supplementary motor area (SMA) and parietal area. However, whether functional networks between M1 and other brain regions such as these motor association areas are related to performance of BMIs is unclear. In order to reveal the relationship between functional connectivity and performance of BMIs, we examined the correlation coefficient between performance of neural decoding and functional connectivity over the whole brain using magnetoencephalography (MEG). Ten healthy participants were instructed to execute or imagine three simple right upper limb movements. To decode the movement type, we extracted 40 virtual channels in left M1 using the beamforming approach and used it as a decoding feature. In addition, seed-based imaginary coherence during real and imagined movements was calculated using frequency components in the alpha band. Seed voxels were set as the same 40 virtual channels in M1. After calculating the imaginary coherence in individuals, the correlation coefficient between decoding accuracy and strength of imaginary coherence was calculated over the whole brain. The significant correlations between imaginary coherence and decoding accuracy were mainly distributed to motor association areas such as the left PMC, inferior and superior parietal lobule (IPL, SPL) and right sensorimotor area in both real and imagined movements. These regions mostly overlapped with brain regions which had significant connectivity to M1. Our results suggested that the strength of functional connectivity between M1 and motor association areas has a potential to contribute to improving the performance of BMIs in real and imagined movements.

P3-070

ON THE DISCOVERY OF PATTERNS OF BRAIN CONNECTIVITY THAT SPAN IN TIME AND FREQUENCY

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Magnetoencephalography (MEG) data is of particular interest for doing research on the functional connectivity of active brain areas due to its fine-grain temporal resolution and non-invasive nature. We aim to use MEG data to identify transient networks of functional connectivity in the brain, discovering interactions between nodes of these networks that change over time and frequency. In short, we aspire to discover the states and dynamics of the system.

The multivariate autoregressive (MAR) model characterises the behaviour of time series by linear historical interactions between the variables or channels. It is well-known that the time domain-oriented MAR model has an unambiguous representation in the frequency domain.

In this work, we take a Bayesian approach that combines a hidden Markov model (HMM) sequence of states with the MAR model for MEG source data modelling (HMM-MAR), so that each HMM state is related to a different set of autoregression coefficients. Therefore, each HMM state can be mapped to a frequency-based representation.

For the nature of MEG data and/or the preprocessing, data are very well described by a single MAR of even moderate order. In order to focus on the actual differences across states we propose to run the HMM-MAR on the residuals of a global MAR model, which encode the common dynamics, which happen to explain a high percentage of the data variance.

Using these techniques, we have been able to discover meaningful networks of activity from real MEG data: 10 minutes of resting state MEG data for nine subjects. Data were frequency filtered into the 4-30Hz band and projected into source space using a beamformer. Results were very consistent across some of the subjects showing encouraging brain symmetry, and revealing interesting, plausible patterns of activity in space and frequency.

P3-071

MODELING AND CORRECTING FOR LINEAR SPATIAL LEAKAGE EFFECTS IN MEG SEED-BASED FUNCTIONAL CONNECTIVITY MAPPING

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Spatial leakage in neuromagnetic inverse modeling represents a fundamental limitation of source reconstruction, especially for seed-based functional connectivity (FC) analyses. The recently introduced orthogonalization method aims at eliminating spurious leakage FC from slow envelope correlation maps. However, orthogonalization makes generic ¬—although not always valid— assumptions on spatial leakage and presents non-trivial biases in envelope FC. Here, we introduce a novel geometric correction scheme that bypasses these limitations, and illustrate it using magnetoencephalography (MEG) resting state data.

Based on a general theory recently developed, a model of linear spatial leakage geometry was derived using the Backus-Gilbert resolving matrix and subtracted from Minimum Norm Estimation (MNE) of source activity. This geometric correction scheme was then tested using resting state data (5 minutes, eyes open) acquired from 15 right-handed adult subjects with a whole-scalp MEG (Elekta, Oy). MNE sources envelope FC analysis was performed using a left primary sensorimotor (SM1) seed (details on data, preprocessing, FC measure and seed location previously published). Group-level FC maps representing the SM1 resting state network (RSN) were then derived using both the geometric correction scheme (FCgeom) and orthogonalization (FCorth).

Both spatial leakage correction methods produced SM1 maps exhibiting typical inter-hemispheric FC that were strongly correlated (spatial correlation: 0.99 (right-hemisphere), 0.97 (left-hemisphere)). A linear relation $FCorth=\xi\times FCgeom$ was found in the right-hemisphere —where no leakage is expected— with slope $\xi=0.815\pm0.007$ (mean±std) over sources. This shows that orthogonalization underestimates SM1 FC and affects resting state envelope FC differently from what has been suggested by previous comparison between orthogonalized and simulated envelope FC values.

These results suggest that both correction methods uncover RSN structures, although orthogonalization introduces biases in envelope FC estimation. The geometric correction scheme appears free of such biases and can actually be applied to any linear inverse model and FC index (e.g., phase coupling).

P3-072
DETECTION PERFORMANCE FOR MEASURING SYNCHRONY – A SIMULATION STUDYING

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Functional connectivity measures have been used to describe a statistical interdependence between two brain areas, suggesting their involvement in a certain brain process. Synchrony in the phase of neuro-magnetic oscillations serves as an indicator of functional connectivity. Recently, numerous algorithms have been developed for measuring synchrony in brain oscillations. Although this approach has provided insightful information about the mechanism underlying brain function, a systematic comparison of how sensitive the different algorithms are in detecting synchrony is still lacking. Moreover, which method perform best seems depending on the nature of the underlying brain signals.

We employed Monte-Carlo randomization and receiver operating characteristics (ROC) for comparing detection performances of common algorithms for measuring synchrony. Sensitivity profiles were derived for detection at alpha equal 0.01. Brain signals were modelled according to an additive interaction between signals as well as phase reorganization (phase reset) without signal power changes.

Results showed an interaction between the models and algorithms. Techniques that consider strictly the phase (e.g PLV) performed better under the phase reorganization model whereas methods that consider the amplitude (e.g MSC) performed better under the additive model.

We used the framework of circular statistic for comparing inter-trial coherence (i.e. the phase differences between a random process and a fixed reference) with coherence between two brain signals (i.e. the phase differences between two random processes). The performance decrease for coherence between two signals was significantly larger than expected from the difference in signal-to-noise ratio between the two cases, suggesting that circular statistics might not be most sensitive for measuring coherence between signals. We are currently expanding the study to algorithms based on non-linear dynamics.

The initial results demonstrate that one must consider how the brain respond during the particular brain function under investigation. Selecting the right algorithm improves detection performance of functional connectivity measurements.

P3-073
QUANTIFICATION OF HIGH-FREQUENCY OSCILLATIONS WITH ACCUMULATED SOURCE IMAGING

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Recent studies have revealed the importance of high-frequency brain signals (>70 Hz). One challenge of high-frequency signal analysis is that the size of time-frequency representation of high-frequency brain signals could be larger than 1 terabytes (TB), which is beyond the upper limits of a typical computer workstation's memory (<196 GB). The aim of the present study is to develop a new method to provide greater sensitivity in detecting high-frequency magnetoencephalography (MEG) signals in a single automated and versatile interface, rather than the more traditional, time-intensive visual inspection methods, which may take up to several days. To address the aim, we developed a new method, accumulated source imaging, defined as the volumetric summation of source activity over a period of time. This method analyzes signals in both low- (1~70 Hz) and high-frequency (70~200 Hz) ranges at source levels. To extract meaningful information from MEG signals at sensor space, the signals were decomposed to channel-cross-channel matrix (CxC) representing the spatiotemporal patterns of every possible sensor-pair. A new algorithm was developed and tested by calculating the optimal CxC and source location-orientation weights for volumetric source imaging, thereby minimizing multi-source interference and reducing computational cost. The new method was implemented in C/C++ and tested with MEG data recorded from clinical epilepsy patients. The results of experimental data demonstrated that accumulated source imaging could effectively summarize and visualize MEG recordings within 12.7 hours by using approximately 10 GB computer memory. In contrast to the conventional method of visually identifying multi-frequency epileptic activities that took 2-3 days and used 1-2 TB storage, the new approach can quantify epileptic abnormalities in both low- and high-frequency ranges at source levels, using much less time and computer memory.

P3-074
OSCILLATORY ACTIVITY ASSOCIATED WITH COGNITIVE MAP GENESIS

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Efficient spatial navigation is of fundamental relevance for adaptive human behavior. However, individuals vary considerably in their ability to generate and derive benefit from cognitive maps for spatial navigation. Inspired by animal and human studies describing hippocampal and prefrontal involvement in relevant epochs of map development as decision making, the present study aims to explore the behavioral and neurophysiological fingerprints of cognitive map development in human subjects.

Healthy participants and epileptic patients implanted with intracranial EEG electrodes participated in a balanced randomized study design based on

the classic taxi driver paradigm. Subjects were assigned to a symmetric and non-symmetric city with reduced landmark information to assess the relationship between navigation variables and space layout in cognitive map generation. Interindividual differences in sense of direction were measured by the Santa Barbara Sense- of- Direction Scale (Hegarty et al., 2002).

Significant low-frequency oscillatory activity within the 2-15 Hz range was found in bilateral parietal and left fronto-temporal sensors during active movement relative to inactive scene viewing. Further analyses are in progress to examine specific neurophysiological correlates of cognitive map development and active versus passive navigation.

P3-075

FUNCTIONAL SYNCHRONY: EXPLORING THE PHASE-COUPLED CORTICAL NETWORKS UNDERLYING SLEEP SPINDLES FROM MEG RECORDINGS

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Introduction: Sleep spindles are transient oscillatory waveforms with dynamic time-frequency features observed during non-REM sleep. They are generated and maintained by a synchronized thalamo-cortical loop that presumably involves different cortical areas over time. The aim of the present study was to develop methodological tools capable of tracking the synchronous functional networks, here called functional synchrony, over time and frequency.

Methods: The methodology is based on non-linear filtering of MEG signals using multivariate wavelet ridge analysis as introduced in Zerouali et al., 2013. This step extracts analytic signal components, called “synchronous events” (SEs) embedding the phase-coupling interactions among sources. We define two classes of SEs: early (first component in each spindle) and late (last component). We then localize the sources of these two classes of SEs and analyse their functional connectivity using PLV measures.

Results: As a replication of previous findings, we found that the instantaneous frequency is high (>13Hz) at spindle onset (early SEs) and low (<13Hz) at spindle offset (late SEs). Sources contributing significant power to early SEs were located mainly in the postcentral gyrus while the one contributing to late SEs were mainly in the precuneus and frontal cortex. The long-range functional connectivity is much denser during late SEs than during early SEs. Interestingly, interhemispheric connectivity is only observed during late SEs. In turn, short-range connectivity was denser during early SEs than during late SEs.

Conclusions: Our methodology provides robust evidence of specific time-frequency patterns in functional synchrony during spindles. Early in spindles, short-range synchrony is strong and long-range synchrony does not display interhemispheric connexions. Importantly, this pattern is reversed later during spindles, where short-range synchrony is decreased and long-range synchrony displays interhemispheric connexions.

P3-076

MAGNETOCARDIOGRAPHY AS PART OF MULTIMODAL NONINVASIVE IMAGING OF MYOCARDIUM IN “DIFFICULT-TO-DIAGNOSE PATIENTS” WITH CORONARY ARTERY DISEASE

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Background: The purpose of this paper is matching of the results of multimodal noninvasive imaging of myocardium, including resting ECG, echocardiography, stress-echocardiography and magnetocardiography.

Materials and methods: The study was conducted in the cardiology clinic of the Main Military Clinical Hospital of Ukraine, Kiev. Three clinical cases of patients with a probable coronary artery disease as determined by intermediate pretests, are presented.

Results: For all three patients the resting electrocardiogram and echocardiogram showed no overt signs of heart disease. At the same time, the results of magnetocardiography and stress- echocardiography in all patients were positive. Hemodynamically significant stenosis was detected in one patient, the other two had stenosis of 50% and 25% respectively.

Conclusion: Multimodal non-invasive visualization of the myocardium, which combines data on global and regional myocardial contractility during rest and exercise as determined by stress- echocardiography and electrophysiological data show that magnetocardiography is a promising diagnostic tool. Further studies are needed to clarify the prognostic value of this hybrid examination.

P3-077

ASSRS IN MEG TO TWO-VOICE MUSICAL FRAGMENTS.

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We measured MEG responses to each voice of simple 2-voice musical fragments of 5 types. Type S had two tones, B5 (990 Hz) and E5 (660 Hz) presented simultaneously and both fixed in pitch for 3 s. In Type H, the higher voice fluctuated as B5-C6-B5-A#5-B5, each tone lasting for 0.5 s whereas the lower voice stayed at E5. In Type L, the lower voice alone fluctuated as E5-F5-E5-D#5-E5. Type P (parallel) had the both voices moving as mentioned. In type AP (antiparallel), the lower voice had E5-D#5-E5-F5-E5 while the higher voice moved as above. The two voices were amplitude modulated separately by sinusoids of 40 and 38 Hz frequencies, thus frequency-tagging the high and low voices. For a control experiment, each voice in each fluctuation form was presented separately. The stimuli were presented to the left ear and ASSRs from the right auditory cortex were measured and band-pass filtered for 1 – 40 Hz. FFT was applied to the averaged responses and 38 and 40 Hz components were analyzed for their differences in power among 5 types of 2-voice fragments. The control experiment showed that the fluctuation in the presented form did not affect the ASSR significantly when a single voice was presented. Compared to

the ASSR to the S stimuli, the other stimuli had inhibitory effects on ASSR power to the lower voice. Effects on the responses to the higher voice were similar in tendency but not significant. The effect of AP was largest of the 4 types having fluctuations in pitch. The results of the control and two-voice experiments showed that the effects of pitch fluctuation emerged through some process of treating the two voices in the auditory system suggesting possible application of this method to investigating neural processes involved in listening to polyphonic music.

P3-078

ULTRA LOW NOISE SQUID SYSTEM FOR ULTRA-LOW FIELD NMR AND MEG

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The ULF-NMR/MRI system developed at PTB uses polarizing fields of up to 50 mT and deploys a single stage DC SQUID current sensor with an integrated input coil. A current limiter consisting of 16 hysteretic SQUIDs is integrated on the SQUID chip. The input coil is connected to a wire wound Nb gradiometer (45 mm diameter, first order gradiometer with 120 mm base line) and the SQUID is housed inside a superconducting Nb shield. The large diameter in conjunction with the large baseline makes the sensor suitable for the detection of deep brain sources. The feedback can be achieved by either feeding back into the input coil or into the SQUID loop itself. Feedback into the input coil will minimize inductive cross talk in multi-channel systems with closely spaced pick-up coils. The single-channel system is operated in our low-noise dewar which has a separation between the inner and outer surface of 8.8 mm (measured at room temperature). With this system we achieve a white noise of ~0.5 fT/√Hz. As we perform ULF NMR/MRI well below 1 kHz, detrimental effects, such as the appearance of additional low frequency noise associated with the application of the large polarizing field, become important. In particular, the material of the wire used for constructing the superconducting pick-up coil is critical in this context. We found a wide spread in the critical magnetic field HC' (the field at which flux penetration into the wire begins) for different wire samples. Consequently, for ULF MR using large polarizing fields, the pick-up coil wire should be screened with regard to HC'. The system is used for very sensitive ULF NMR at frequencies below 1 kHz and also for ultra sensitive MEG recordings.

P3-079

FLUX-TRAPPING IN TYPE-II SUPERCONDUCTING PICK-UP COIL AND PREPOLARIZING COIL DUE TO STRONG MAGNETIC FIELD FROM THE PREPOLARIZING COIL

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Recent efforts in the development of Ultra-Low Field Nuclear Magnetic Resonance (ULF-NMR) mainly focus on increasing prepolarizing field (Bp) strength. Strong Bp is mandatory for producing high-quality NMR signals. However, this strong Bp also poses a technical difficulty since it needs to be rapidly and completely removed so that spin relaxation signal measurement can take place before the sample magnetization wears off. Vesanen et al. [1] reported that a superconducting Bp coil producing 22 mT or more resulted in magnetic flux being trapped inside the superconductor. This trapped flux, after Bp is removed, produced a stray magnetic field, resulting in suppressed spin relaxation signals and image distortions. This could also happen to the SQUID pick-up coil, which is made of Nb or NbTi, both of which are type-II superconductors and susceptible to flux-trapping under a strong magnetic field. We present a comparison study with three pick-up coils made of Nb, NbTi, and Pb, where we found that only the pick-up coil made of Pb, a type-I superconductor, was unaffected by the strong magnetic field from the Bp coil and produced sharp NMR signal whose amplitude scaled linearly with Bp. The type-II coils, under strong magnetic fields, suffered from shorter and suppressed spin relaxation signals with broader spectral peaks. [2] Further, a counter pulse of opposite polarity following the Bp pulse removed the trapped flux and recovered the spin relaxation signal. A superconducting Bp coil can only be made of type-II superconductors due to its high critical field requirement. We discuss ULF-NMR/MRI pulse sequences incorporating suitable Bp counter pulses to neutralize the flux trapped inside the Bp coil, increasing the Bp limit.

[1] P. T. Vesanen et al., Magn. Reson. Med. 69, 1795 (2012).
[2] S.-m. Hwang et al., Appl. Phys. Lett. 104, 062602 (2014).

P3-080

THE ELECTROMAGNETIC FIELD OF TMS PULSES IN NON-TARGETED REGIONS: IMPLICATIONS FOR SAFETY

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In transcranial magnetic stimulation (TMS), a strong magnetic field pulse is used to stimulate neurons in the brain of the subject. The peak magnetic field strength of a TMS pulse may exceed one tesla, and the mean power during a pulse is in the order of several megawatts (the pulse lasts only 100–400 µs). In a stimulation session, the operator holds the TMS coil against the subject's scalp, the coil then being at a distance of 10–20 mm from the cortex. In the cortex, a TMS pulse induces an electric field whose peak amplitude is typically 50–100 V/m.

In addition to stimulating the subject's cortex, the TMS pulse may affect also nearby tissues and other objects. These include the subject's scalp, cranial muscles, heart, and the fetus of a pregnant subject as well as the TMS operator and any devices worn by the subject or operator such as cardiac pacemakers or hearing aids. The stimulus intensity in these have been studied only a little; although, for example, the TMS operator is often very close to the TMS coil: holding the coil (coil–finger distance less than 10 mm) in a stable fashion close to his or her body (coil–torso distance can be below 200 mm).

We will present the TMS-induced electric and magnetic field strengths in non-targeted tissues for typical TMS coils and compare these to the ICNIRP guidelines for time-varying electromagnetic fields. We raise the question in which cases these TMS-induced electromagnetic fields may cause a safety hazard.

P3-081

THE RELAXATION MEASUREMENT OF BREAST CANCER TISSUE BY USING SQUID-BASED LOW FIELD NMR

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A T1-contrast image without a contrast agent is obtainable at low field by using a SQUID-based micro-Tesla NMR/MRI. Since the various natural frequency modes by molecular motion can influence the relaxation time, we measured the T1 of the normal tissues and the tumor tissues of 15 patients with breast cancer in ex-vivo by the micro-Tesla NMR at three different fields below 122 μT in order to investigate the multi-frequency T1 pattern according to the magnetic field and capability for obtaining of T1-contrast image. Since the tissues have a small volume, the signal reconstruction method based on Bayesian analysis was adopted to overcome the low signal-to-noise ratio. However, there were no meaningful T1 tendencies at the three different fields, except for the mucinous carcinoma. An enhanced T1 contrast was obtained at the mucinous cancer tissue, which was more than 4. The result of the simulation for minimizing the error generated by the time interval suggested that it is important to get the first time point of the T1 measurement as short as possible and the equally spaced time interval.

P3-082

EFFECTIVE ON- AND OFFLINE METHODS FOR REMOVING TMS-RELATED EEG ARTIFACTS

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Combined transcranial magnetic stimulation (TMS) and electroencephalography (EEG) is a unique method for studying the connectivity of the brain. With neuronavigated TMS (nTMS), it is possible to induce activation accurately in a desired location on the cortex. Furthermore, by combining nTMS with simultaneous EEG, one can measure directly how the TMS-evoked activity spreads in the brain due to axonal transmission.

Combined nTMS–EEG is methodologically a challenging technique. In addition to inducing a stimulating electric field inside the brain, the strong and rapidly changing TMS pulse is prone to generate large artifacts in the EEG signal. These artifacts can be both physiological, e.g., large biphasic deflections resulting from the twitching cranial muscles, and technical, e.g., electrode–skin interface depolarization.

We discuss how artifacts can be minimized in online situation by appropriately altering the following stimulus parameters: coil location, intensity, and coil orientation. Furthermore, we have developed an effective signal-processing algorithm which can be used offline to remove large TMS–EEG artifacts. In the algorithm, we suppress the artifacts in the EEG sensor space by using the signal-space projection method. After the suppression, we use the remaining EEG information to solve the cortical activation creating the cleaned signals. Finally, the solved activity pattern is projected on the original signal space by using the anatomical information of the subject.

The results show that by choosing the stimulation parameters appropriately, we are able to measure clean EEG signals. However, this choice of parameters forces us to stimulate the cortex relatively close to the midline of the head. By using the presented signal processing algorithm, we are able to stimulate also with such parameters that produce artifacts. This increases the versatility of combined TMS–EEG significantly. The presented offline approach can also be used in magnetoencephalography and other EEG studies.

P3-083

TOWARDS MICRO-MAGNETIC STIMULATION OF AUTONOMIC NERVOUS SYSTEM ~DEVELOPMENT OF IN VITRO MODEL SYSTEM~

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The autonomic nervous system plays an important role in the function of living things. Several diseases such as heart failure occur when the homeostasis of the autonomic nervous system is unbalanced. To treat these diseases, it is useful to control the activity of the autonomic nervous system. However, today's control methods are invasive such as electric stimulation with electrodes implanted in the body. Using a new treatment method we can control from outside the body. In recent years, magnetic stimulation has focused on non-invasive stimulation methods. There is some possibility of controlling the activity of autonomic nervous system by magnetic stimulation. However, it is difficult to control this at the cellular level. Our aim is to establish a method of magnetic stimulation at the cellular level in vitro. The previous study showed a co-culture system of sympathetic neurons and cardiomyocytes. However the co-culture system of parasympathetic neurons and cardiomyocytes has not been developed. In this study, we developed and evaluated the co-culture system of parasympathetic neurons and cardiomyocytes. Rat intracardiac ganglion (ICG) neurons and atrial myocytes (AMs) were co-cultured in a chamber with two culture compartments and pathways between these compartments. A chamber was placed on a microelectrode-array substrate and connected with pathways. To confirm that the ICG neurons

and AMs are functionally connected, we applied electrical stimulus to the ICG neurons. Beat intervals of AMs significantly increased by 12.3±6.01% after stimulation and there was no significant difference in beat intervals between before and after stimulation in the presence of atropine (Muscarinic acetylcholine receptor antagonist). These results suggest that functional synaptic connections were formed between ICG neurons and AMs. In the future study, we are going to develop the tri-culture system of sympathetic neurons, parasympathetic neurons and cardiomyocytes and aim to control the autonomic nervous system by magnetic stimulation.

P3-084

A 375-CHANNEL PEDIATRIC "BABYMEG" SYSTEM: DESIGN AND BASIC PERFORMANCE

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We describe the design and basic performance of the 375-channel pediatric MEG system ("babyMEG") being developed for Boston Children's Hospital. The sensor array uses a dual-layer design consisting of 270 radial magnetometers (10 mm diameter circular coil, spaced 15 mm apart) in the inner layer and 35 units of 3-axis magnetometers (20 mm in diameter) in the outer layer with a distance (baseline) of 40 mm between the two layers. There are an additional set of 9 reference magnetometers arranged in such a way that pairs of magnetometers can be combined into a complete 3x3 tensor of gradiometers. The sensor array can be finely positioned on site by the users to obtain a minimal gap of ~7-8 mm between the magnetometers in the inner layer and the outer helmet surface. The SQUID electronics are capable of removing the dc field to increase the dynamic range of the system. A set of filters and amplifiers enables optimal adjustments of the gains and bandwidth with a sampling rate of up to 5 kHz/channel. The digital electronics have a 24-bit resolution. The system comes equipped with a 100% liquid helium recycler. This system will be installed in the new MEG facility at the Children's in May. We have developed several methods of noise cancellation since the system consists of magnetometers only in an economical 2-layer magnetically shielded room (MSR) with a thin separation between the two layers (Vacuum Schmeltz Basic Plus) in a clinical area on the 7th floor of the main hospital building. The methods include passive shielding, external and internal active shieldings using a feedback mode of operation, synthetic gradiometer, a 9-channel reference system with 3 x-y-z magnetometers and 6 gradient tensors, and real-time signal space projection (SSP) and real-time signal space separation (SSS). This noise cancellation scheme is expected to reduce the noise levels sensed by each synthetic gradiometer to <10 fT/ÖHz down to 0.1 Hz. The ac-coupled filter should reduce the noise level to <1 fT down to 0.1 Hz. The system noise level is expected to be ~8 fT/ÖHz for the inner- and ~4 fT/ÖHz for the outer-layer magnetometers. Single-epoch detection of evoked cortical activity should be possible with the short minimum gap of ~8 mm between the magnetometers and the scalp and the predicted noise level. If the babyMEG operates according to these calculations, it should be possible to study normal and abnormal electrophysiological human brain development below 3-4 years of age with unprecedented levels of sensitivity and spatial resolution.

P3-085

COMPARISON OF SOURCE ESTIMATION OF ICTAL AND INTERICTAL EPILEPTIC DISCHARGES BETWEEN MEG AND DEEG

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Recent reviews suggest simultaneously recorded MEG and EEG may maximize the advantages of each for presurgical epilepsy evaluations compared to either modality alone. Both EEG and MEG have the advantage of recording rapidly changing signals and limitations: for MEG limitations include the requirement to limit head movement, for EEG limitations include distortion of signal by skull impedances and other cranial tissues. For source level, MEG is more sensitive to tangential sources whereas EEG is more sensitive to radial sources. We aimed to determine the value of simultaneous MEG and dense array EEG (dEEG) for characterization of the epileptogenic zone in pediatric intractable focal epilepsy.

We recorded simultaneous MEG with 275 sensors and dEEG with 256 or 128 electrodes, depending on the patient's head circumference, from 3 pediatric patients who were undergoing non-invasive epilepsy presurgical evaluation. MEG and dEEG recordings were synchronized within 1/1000 second level accuracy. Ictal events were captured from 2 patients, and interictal discharges were observed from all 3 patients. The source estimations for both ictal onsets and interictal discharges were assessed with CURRY 7 software using 5 different algorithms including ECD, MUSIC, MNE, sLORETA and SWARM within the frequencies determined by wavelet time frequency analysis. The boundary elemental model (BEM) segmented from each patient's own MRI was the head model.

In this first small subject sample we found that the combined use of whole-head MEG and dEEG in conjunction with advanced source modeling techniques promotes better noninvasive characterization of both the irritative regions and ictal onset zone in presurgical epilepsy evaluations with observation of the different directions of sources between MEG and dEEG. In addition, using frequency domain analysis judiciously, i.e., frequency bandwidths tailored to the signal properties rather than the fixed broad conventional bandwidths gathers more information that is relevant to invasive recording findings.

P3-086
VISUAL EVOKED FIELDS — RELATING TO APPARENT MOTION ILLUSION

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The aim of this study was to examine visual evoked fields in magnetoencephalogram (MEG) associated with the perception of classical apparent motion illusion (beta movement). A pair of 3-dimensional spheres was, left/right and right/left visual field, presented 10.1 degrees apart from each other horizontally. The first sphere of a duration of 16.7 ms was followed by the second one in combination with two condition of stimulus-onset-asynchrony which resulted in two different percepts: 16.7 ms, almost the two spheres seen simultaneously: 66.8 ms , perceived beta movement optimally. In addition, spheres of 128 were presented animatedly as those produced a real motion percept. The MEG was measured from 10 healthy participants with a 122-channel whole-head MEG system in a magnetically shielded room. Results were as follows: A greater activation was observed for the percept of beta movement than that of simultaneous in the occipital, temporal and frontal regions. The peak latency in the occipital region was shorter than that of the others, and the peak latency in the temporal region was comparative to that in the parietal region. The latency of contralateral responses to the first stimulus (ipsilateral to the second stimulus) was shorter than that to the second stimulus (ipsilateral to the first stimulus) in the occipital and parietal regions. In contrast, in the temporal region, the latency of contralateral responses to the second stimulus was shorter than that to the first stimulus. These results suggest that the MEG activity at the temporal region may relate to the percept of the motion.

P3-087
QUALITY-CONTROL AND OPTIMAL SPECTRAL RECONSTRUCTION OF OSCILLATORY PARAMETERS IN STUDIES OF INDIVIDUAL VARIABILITY AND PHARMACO-MEG

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There has been much recent interest in the use of oscillatory biomarkers, such as induced visual gamma frequency/amplitude, as probes of local synaptic physiology. It is thought that these may represent functionally relevant indices that correlate with individual variability in neurochemistry, behavioural performance and may reflect specific impairments of synaptic function in diseases such as Epilepsy and Schizophrenia. In addition, many recent studies have demonstrated their utility in providing neurotransmitter-specific targets for pharmacological manipulation [1]. However, successful interpretation of both studies of individual variability and pharmacological intervention requires both an optimised approach to spectral characterisation and robust, unbiased and automatic methods for rejecting poor-quality data. Here we describe an analysis framework that uses bootstrapping across trials to provide confidence estimates on both oscillatory amplitude and frequency, and show how these can be used to assess data quality. These methods also allow an evaluation of a variety of spectral estimation tools, both parametric and non-parametric to inform the optimal choice of method. Here we apply these approaches to four different studies of individual variability in visual gamma frequency (a total of 160 participants). The best performing spectral estimation method was a parametric AR-based technique – the modified covariance method. This identified 75% of the participants as having a robustly estimated gamma peak. We applied the same quality-control/spectral estimation approach to a pharmaco-MEG study using the GABA reuptake inhibitor, Tiagabine, in which we previously had demonstrated a null finding [1]. Out of an initial 15 participants, our quality-control method identified 9 in which gamma was robustly characterised across all eight placebo/drug runs. Using these data, in contrast to our previous null finding, we observed a clear reduction in visual gamma frequency with Tiagabine, compared to placebo, demonstrating the importance of appropriate quality-control measures in pharmaco-MEG.

[1] Muthukumaraswamy, et al. (2013). Neuropsychopharmacology, npp.2013.9.

P3-088
CAN MEG DISTINGUISH SUBCOMPONENTS OF THE GABAERGIC SIGNALLING SYSTEM?

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In these studies we compare the specificity of MEG spectral responses to three GABAergic drugs, each with highly specific and distinct mechanisms of action. These included the GABA-A benzodiazepine positive allosteric modulator zolpidem which enhances phasic GABA currents, the delta subunit selective agonist gaboxadol (THIP) which enhances tonic currents and the GABA reuptake inhibitor tiagabine, which potentially upregulates both types of current. The waking MEG/EEG of gaboxadol (unlicensed) has not yet been described in man. These three studies were randomised, single-blind, placebo-controlled, crossover studies in healthy volunteers with baselines. In the zolpidem (10 mg) study there were twelve volunteers, in the gaboxadol (15 mg) study ten volunteers and in the tiagabine (15 mg) study fifteen volunteers. Five minute resting-state MEG recordings were made for each. Following artefact rejection, data was converted to planar gradient configuration, and frequency analysis conducted. Individual spectra were divided into the following frequency bands, delta (1 - 4 Hz), theta (4- 8 Hz), alpha (8 - 13 Hz), beta (13 - 30 Hz), low gamma (30 - 50 Hz) and high gamma (50 - 100 Hz) with baseline spectra subtracted from each post-intervention spectra and differences compared to placebo. The findings for zolpidem were as previously reported in EEG studies, with significant increases in beta frequencies and reduction in alpha frequency power; for gaboxadol and tiagabine there

were significant increases in power at all frequencies up to beta. Thus the enhancement of tonic inhibition via extrasynaptic receptors by gaboxadol gives rise to a different MEG signature from the synaptic action of zolpidem. The similarity of results for tiagabine and gaboxadol suggests with tiagabine at this dose, overspill of neurotransmitter occurs from the synapse to generate this spectral change. In conclusion, MEG can provide distinct spectral signatures to highly specific alterations of the GABA subsystem.

P3-089

GAMMA-BAND MODULATION IN THE AMYGDALA DURING EMOTIONAL FACE PROCESSING IN RESPONSE TO KETAMINE

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The NMDA antagonist ketamine produces rapid anti-depressant effects, observed within hours of administration. Interestingly, while much is known about the cellular and neuron level effects of NMDA antagonism, little is known about the large-scale neural effects and mechanisms by which ketamine exerts antidepressant effects.

We investigated neural responses with MEG during an emotional evaluation task involving identification of either the gender or the emotion of faces in 17 subjects with major depressive disorder (MDD), after both placebo and 0.5mg/kg ketamine infusions administered in a double blind crossover design. Four ninety-second blocks of time during emotional (explicit emotion processing) and gender (implicit emotion processing) identification were transformed into source space via synthetic aperture magnetometry [1] and contrasted in order to obtain gross power differences between the conditions. A linear mixed effects model was utilized for voxel-level statistics, and correction for multiple comparisons was made using Monte Carlo simulations. Significant differences in gamma power were observed between explicit and implicit emotion processing after ketamine infusion in the amygdala as compared to placebo ($p<.01$ $\alpha<.01$).

Gamma frequency involves the balance of excitation and inhibition in multiple cell types [2], and NMDA antagonism has been shown to impact gamma-band activity in evoked and passive processing [3,4,5]. Interestingly, here we show that amygdala gamma-band activity is modulated differentially between explicit and implicit processing of emotional faces after ketamine administration. We hope this research will aid to further understand the neural underpinnings of ketamine's anti-depressant effects.

[1] Robinson and Vrba, 1999.
[2] Siegel et al., 2012
[3] Cornwell et al., 2012
[4] Lazarewicz et al., 2010
[5] Lahti et al., 2010

P3-090

ABNORMALITIES IN SYNCHRONY AND ENTROPY IN PSYCHOSIS

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Introduction: Abnormalities in visual and motor processing are well-documented in patients with psychosis1,2. In addition to traditional spectral analysis of MEG data, measures of signal entropy describe the level of complexity in the signal. This study aimed to investigate spectral and complexity differences between patients with psychosis (N=19, medicated) and control participants (N=28) in a simultaneous visual and motor task.

Methods: Participants pressed a button whilst viewing a visual grating for two seconds, then maintained fixation for a seven second baseline period. Data were recorded using a 275 sensor CTF MEG system. Locations of peak motor beta (13-30Hz) power decrease and visual gamma (30-70Hz) power increase during stimulation were identified using a scalar beamformer and virtual electrodes were computed at these locations. The percentage difference from baseline in the amplitude envelopes of oscillatory signals in these frequency bands was calculated. Finally, rank vector entropy (RVE)3 was computed at the same locations using broadband (1-150Hz) data.

Results: Patients exhibited enhanced beta power decreases in motor cortex during the movement and reduced post movement beta rebound ($p_{corrected}<.05$). Visual gamma was not significantly different between patients and controls. RVE at the same locations showed similar results, with patients exhibiting a larger increase in entropy during movement and a smaller post-movement decrease ($p_{corrected}<.05$).

Discussion: The findings from spectral and complexity analyses indicate abnormal neuronal processing in the motor cortex in patients with psychosis. The overall reduction in synchrony and increase in entropy in patients suggests disorganisation of local neuronal networks that prevents optimal reactions to stimuli. The findings show promise for a simple and brief MEG task to be used as a biomarker for psychosis.

[1] Butler et al (2008) Biological Psychiatry
[2] Whitty et al (2009) Schizophrenia Bulletin
[3] Robinson et al (2012) Frontiers in Computational Neuroscience

P3-091

AN MEG STUDY OF MOTOR-RELATED BETA OSCILLATIONS DURING MOTOR IMITATION IN AUTISM

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As early as 20 months of age, children with autism exhibit robust imitation impairments. Diverse explanations have been proposed, including motor

and sensory perception control deficits. Abnormalities in motor-induced cortical rhythms have been reported in ASD adults while performing motor imitation tasks, however, children haven't been investigated yet.

Neuromagnetic oscillatory changes within the beta frequency band (15-30 Hz) were calculated during finger-lifting movements in 11 ASD and 12 control children. Decreased beta power (ERD) was observed prior to and during the movement and imaged using a -500-500 msec time window (0 being the onset of the movement). Following the movement, an increase in beta-band power (PMBR) was imaged using a 700-2000 ms time window. PMBR and ERD of each group were compared at the sensor level in each hemisphere and subjected to group statistical analysis using a 2 samples t-test.

As expected, we found relevant motor-associated beta oscillations in both hemispheres. In the contralateral hemisphere, ERD was significantly more robust in the autism group compared to the controls for both index (p=0.01) and little (p=0.03) movements. In contrast, PMBR might have been reduced in ASD subjects, although it did not reach statistical significance, during imitation of index (p=0.06) and little (p=0.07) lifting movements. In the ipsilateral hemisphere, no group difference was found in the beta-band independently of the movement performed.

These results provide some physiological evidence of distinct brain activity associated with imitation of hand movements in children with autism. It is possible that the greater ERD in autism was due to increased motor and/or imitation planning difficulty. PMBR is generally associated with motor deactivation or inhibition and has been correlated with GABA concentration within the brain. The reduced PMBR in autism is interesting in light of a recent study showing decreased GABA level in the motor cortex in ASD.

P3-092

AUDITORY ENCODING ABNORMALITIES IN SCHIZOPHRENIA: ASSOCIATIONS WITH GRAY-MATTER CORTICAL THICKNESS AND ATTENTION

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Although studies indicate abnormalities in multiple nodes of a concurrently activated auditory network in individuals with schizophrenia (SZ), the functional consequences and the neuroanatomy associated with aberrant auditory processing in SZ are not fully understood. The present study evaluated how auditory encoding network node activity is associated with attention and brain structure in SZ and healthy controls (HC).

MEG measures of auditory encoding (click stimuli) were obtained from 69 SZ and 70 HC. Vector-based Spatial-temporal Analysis using L1-minimum-norm (VESTAL) provided whole-brain maps of activity from 80-130ms (M100). Gray-matter cortical thickness (CT) and a composite measure of attention (averaging z-scores from Digit Span Forward, Spatial Span Forward, and CPT Clinical Index) were also obtained.

HC showed stronger M100 activity than SZ in left and right superior temporal gyrus (STG) as well as in right prefrontal regions (R-Frontal). SZ showed stronger activity in left superior frontal gyrus (L-SFG) than HC. Hierarchical regressions showed that increased M100 L-STG and R-Frontal activity (areas where HC > SZ) was associated with better attention (for L-STG this relationship observed only in HC). In contrast, increased L-SFG M100 activity (area where SZ > HC) was associated with poorer attention. Finally, SZ had less CT in regions where HC showed stronger M100 activity than SZ, and in those regions increased CT was associated with stronger M100 activity (for L-STG this relationship observed only in HC).

Encoding abnormalities in SZ - too little activity in STG and R-Frontal regions and too much activity in L-SFG regions - were associated with CT abnormalities and poorer attention. Stronger L-SFG activity in SZ perhaps indicates an attempt to compensate for STG auditory encoding impairments, with those individuals with SZ showing the greatest encoding impairments (weakest STG and strongest L-SFG M100 activity) showing the greatest attention impairments.

P3-093

THE EFFECTS OF ESZOPICLONE ON SLOW WAVE MODULATION OF SLEEP SPINDLES IN SCHIZOPHRENIA

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The temporal coordination of sleep spindles (12-15Hz) with slow waves (SW; 0.5-1.5Hz) is thought to contribute to memory consolidation during sleep. In schizophrenia, there are marked reductions in spindle activity and sleep-dependent memory consolidation, and these deficits are correlated. Eszopiclone (Lunesta) increases spindle activity in schizophrenia. We investigated whether eszopiclone also normalizes SW-spindle interactions.

Twenty-one chronic, medicated schizophrenia outpatients were randomly assigned to receive either placebo (N=11) or 3mg of eszopiclone (N=10) on two consecutive nights of polysomnography. On the second night, they were trained on the finger-tapping motor sequence task (MST) at bedtime and tested the following morning. Stage 2 sleep spindles occurring on the upstate of the SWs were classified as SW-modulated. SW-triggered spectrograms and coherograms quantified SW coordination with spindles.

Compared to placebo, eszopiclone significantly increased both non-SW-modulated sigma power and sigma power that was time-locked to the upstate of slow waves ($F_{1,19}=27.02$, $p<0.0001$). Moreover, SW-modulated

spindles were more coherent across EEG channels in patients taking eszopiclone versus placebo ($F_{1,19}=42.44$, $p<.0001$). In the eszopiclone group, coherence in the sigma-band was greater during the sleep that followed MST learning than during the preceding night ($F_{1,19}=12.08$, $p<.0005$), suggesting that spindle coherence is enhanced by learning.

In addition to increasing sleep spindle density, eszopiclone increased both the power and the coherence of SW-modulated sigma activity in schizophrenia. Since EEG and MEG are differentially sensitive to spindle types, we are now using simultaneous high-density EEG and MEG recordings to fully characterize the interaction between SWs and spindles, its relation to memory consolidation, and how this goes awry in schizophrenia. Furthermore, we will compute current source estimates of SW and spindle waveforms, anatomically constrained by structural MRI, to identify brain circuits involved in sleep-dependent memory consolidation. We will present both the eszopiclone data and preliminary MEG-EEG measurements of SW modulation of spindles.

P3-094

USING MEG TO EXAMINE TOP-DOWN REGULATION IN FIBROMYALGIA

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Fibromyalgia Syndrome (FMS) is a disorder characterized by the presence of widespread pain and tenderness, which is now believed to be, at least in part, a disorder of central pain processing producing hyperalgesia and allodynia. These phenomena might be caused by defective top-down sensorimotor regulation. In order to test this notion, we activated the pain matrix in a top-down manner by presenting pictures of painful situations while recording brain activity using MEG. We hypothesized that FMS patients will show different responses to pain pictures and will not show normal alpha desynchronization. We tested 19 FMS patients and 14 age-matched healthy controls (age 30-50). In healthy controls exposure to pictures depicting painful situations induced a decrease in alpha activity (10-12Hz) which was significantly more pronounced than the one induced by non-painful content. However, FMS patients did not show decreased alpha for pain relative to no-pain pictures, indicating abnormal regulation of sensorimotor cortex. Analysis of the event-related activity showed that, in controls, pain pictures elicited lower activity relative to non-pain pictures in precentral and post-central gyri, precuneus and superior parietal lobule. FMS patients showed the opposite effect, eliciting greater activity for pain-depicting pictures in the same areas. In addition, FMS patients showed overall greater activity in medial frontal and supplementary motor areas evident at early processing stages. Our findings suggest that defective top-down regulation may play a role in the pathogenesis of FMS.

P3-095

THE TIMING OF AUDITORY VERBAL HALLUCINATION NETWORKS IN SCHIZOPHRENIA

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Introduction: The costs of Auditory Verbal Hallucinations (AVH) to patients with schizophrenia (SP) are devastating. Understanding AVH brain network functioning is essential to solving the problems of AVH. Regions involved in AVH include inferior frontal gyri, insula, the superior temporal gyri, and the inferior parietal lobule. The purpose of the present study was to evaluate the relative timing of these regions in an AVH network.

Method: Twenty adult SP with AVH were scanned as part of a larger study. During a MEG-scan, SP were instructed to respond with their right index finger when AVH began and with their left index finger when AVH ended. Approximately 1800 seconds of MEG-data were collected from each SP using a whole-cortex 306-channel MEG array. After standard offline preprocessing, epochs for AVH onset and offset were constructed using 1.5 seconds after the respective motor responses. Using MNE-python, phase slope index (PSI) was computed relative to superior temporal sulcus (STS) for AVH onset and offset in the theta and alpha bands. Individual PSI estimates were registered to the MNI template brain using a spherical morphing procedure and compared using paired t-tests.

Results: In the theta band, significant PSI differences were detected for left middle frontal gyrus (offset>onset), superior frontal gyrus (onset>offset), inferior temporal gyrus (offset>onset), and right orbitofrontal cortex (onset>offset). In the alpha band, significant PSI differences were detected for left middle fontal gyrus (onset>offset), inferior temporal gyrus (onset>offset), and right middle frontal gyrus (onset>offset).

Conclusion: Using a measure of directed influence (PSI: Nolte et al. 2008) to examine the timing of AVH network activity in SP, the timing of oscillatory activity in STS differed significantly for the period of transition into AVH relative to transition from AVH into a non-AVH state. Future work will evaluate whether this activity can be modulated using brain stimulation.

P3-096

ALTERED PROCESSING OF EMOTIONAL CONFLICT IN PMDD: A MEG STUDY

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The prevalence of premenstrual dysphoric disorder (PMDD) is about 3-8% in women of reproductive age. The mood liability and emotional

dysregulation in PMDD patients severely impact their social function and life quality. This study investigated the emotion perception and regulation in PMDD patients in order to elucidate brain pathophysiology. Twenty PMDD women and nineteen normal female controls were enrolled in this study. The MEG was recorded under an emotional face-word Stroop task (judgment of facial expression, angry or happy) during PMDD's symptomatic pre-menstrual and symptom-free post-menstrual periods, respectively. The peak amplitude and latency of evoked magnetic fields (EMFs, sensor level) at ~170 ms from four channels-of-interest (covering Broca's, anterior cingulate cortex (ACC), left fusiform, and right fusiform areas) were extracted from each subject. Two-way ANOVA with repeated measurement (group x phase) were conducted for each area. The results of behavioral data (accuracy and response time) showed neither main effect nor interaction between group and phase. Analysis of EMFs disclosed significant interactions for the latency at the right fusiform area ($F(1,120)=11.88$, $p=0.001$) and left fusiform area ($F(1,120)=5.16$, $p=0.025$), and the amplitude at Broca's area ($F(1,120)=5.5$, $p=0.02$) and ACC ($F(1,120)=6.77$, $p=0.01$). The findings of faster perceptual processing and increased emotional conflict monitoring processing in patients with PMDD after menstrual phase indicated modulation of hormone on neural processing of affective information in PMDD. We will discuss in this report our data of both sensor space and source space in the context of altered perceptual processing and emotional conflict monitoring.

P3-097

EXAMINING NEURAL SYNCHRONY IN AUTISM SPECTRUM DISORDERS WITH MAGNETOENCEPHALOGRAPHY (MEG) DURING RESTING STATE

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Autism spectrum disorders (ASD) are marked by social cognitive impairments. Abnormalities in synchronous neural activity vital to connectivity have been suggested as a core pathophysiological mechanism. The Default Mode Network (DMN) believed critical for internal tasks such as taking others' perspectives is active during resting state. We hypothesized there would be decreased coherence between cortical regions of the DMN (e.g. frontal) and other regions coupled with increased posterior synchronous activity in ASD consistent with their often-noted perceptual-cognitive style.

Cortical activity was recorded in five age- and gender-matched male children with and without ASD (Mean age = 9.0; SD = 1.0) using 148 channel whole head MEG during resting state. Data were band-pass filtered 3-85 Hz, digitally sampled at 508.63 Hz, and artifacts eliminated with ICA. Synchronization of neuronal activity was quantified by calculating coherence between cortical sites from MEG imaged activations. Cortical coherence levels were used to quantify differences in connectivity. Power spectra for active sites were calculated. A region-of-interest tool was used to identify 54 regions in the brain.

We compared the top three regions of neural activity between groups. Collapsed across frequencies, ~80% of the regions activated were frontal in NTs compared to ~20% in ASD. Minimal differences in the alpha or beta bands were noted. A higher percentage of posterior gamma frequency band oscillatory activity was noted in ASD. In NTs, ~60% of the cortical regions with the highest gamma activity were frontal and ~40% were posterior regions while ASD displayed a reversed pattern (~40% frontal, ~60% posterior).

Higher gamma oscillatory activity at rest in medial frontal regions associated with the DMN was noted in NTs. Higher posterior gamma oscillatory activity was noted in ASD, particularly in temporal, parietal, and occipital lobes. Altered synchronization in the DMN may contribute to the behavioral phenotype.

P3-098

INVESTIGATING SENTENCE-LEVEL AUDITORY DISCRIMINATION IN AUTISM WITH MAGNETOENCEPHALOGRAPHY

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Typically developing children rely on context to guide their everyday perceptions and for flexible behavior. In contrast, children with autism spectrum disorder (ASD) present with rigid and stereotyped behaviors, evident in their verbal responses. The present study investigates sensitivity to semantic context using an N400 event-related paradigm incorporating phonological foils (i.e., phonetically similar, PS, vs. phonetically dissimilar, PD, to sentence-terminal target words) with a view to understanding language deficits in ASD. Using whole head magnetoencephalography (MEG), we compared the brain activation patterns of high functioning children with ASD (IQ > 75) with age- and IQ-matched controls, 13-16 years of age, performing a sentence-level auditory discrimination task. Event-related responses to the terminal word in each sentence condition (congruent, similar and dissimilar) were averaged and analyzed using a distributed source solution, the Minimum Norm Estimate. Preliminary results revealed no significant difference between the groups in accuracy on the task (mean accuracy: 92%). However, the ASD group was faster at rejecting the PD than the PS foils, whereas the control group had similar reaction times on both foils. Furthermore, MEG findings yielded a weaker and primarily left-lateralized response in the PS than in the PD condition in posterior temporal areas for control subjects. In comparison, children with ASD showed stronger and more persistent activity in the PD than PS condition in middle and inferior temporal areas in the left hemisphere. The contrasting response patterns of the two groups suggest differences in engagement of language circuitry between the groups.

P3-099
PHYSIOLOGICAL INDICATORS OF MULTISENSORY FACILITATION IN SCHIZOPHRENIA

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Auditory and visual deficits have been consistently reported in patients with schizophrenia, with more recent studies providing evidence of either direct or indirect influences of sensory deficits on cognitive abilities. However, interactions within the real world are multisensory in nature, and thus more emphasis should be placed in understanding multisensory integration. Based on the poor connectivity hypothesis of schizophrenia, we hypothesized that patients with schizophrenia (SP) would show impaired multisensory integration relative to healthy controls (HC). We investigated multisensory responses using a forced choice auditory/visual multisensory paradigm, where participants responded to spatial location of unisensory auditory, unisensory visual and simultaneous auditory and visual stimuli in a fully randomized design. Evoked responses were measured using an Elekta Neuromag 306 channel MEG system, and were preprocessed to remove artifacts. Source analysis was performed and the resulting source locations and timecourses were evaluated. For our current analysis, we identified the peak latencies of the timecourses from dipole sources in visual cortex in response to unisensory visual and multisensory stimulus conditions. Based on a mixed model repeated measures design, a significant interaction ($p = 0.001$) of group (SP versus HC) by condition (unisensory visual stimulus, multisensory stimulus) was identified. Consistent with behavioral results indicating greater multisensory facilitation in SP relative to HC, SP had slower visual peak latencies relative to HC in response to unisensory visual stimuli, yet faster visual peak latencies than HC in the multisensory condition, indicating facilitation of the cortical visual response. This result is consistent with our previous studies indicating a similar facilitation of the evoked auditory response in SP relative to HC. Contrary to our initial hypothesis, the results indicate that individuals with schizophrenia may compensate for unisensory deficits through multisensory stimuli; this result may provide a target for improving outcomes in schizophrenia.

P3-100
TRANSCRANIAL MAGNETIC STIMULATION USING FIGURE-OF-EIGHT COIL WITH BENDING WINGS

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Transcranial magnetic stimulation (TMS) is a noninvasive technique to stimulate the brain. In TMS, stimulation coils located near the scalp produce magnetic fields that in turn induce electric fields and eddy-currents in the conductive brain tissues. TMS has hold significant promise as a tool for cognitive neuroscience and the treatment of neurological disorders

The first TMS system used a circular coil due to its simple geometry and ease of construction. However, the circular coil induces a non-focal ring-shaped electric field. The significant improvement of TMS focality has been realized by the introduction of the figure-of-eight (fo8) coil.

The fo8 configuration consists of a pair of adjacent circular loops with current flow in opposite directions, producing a relatively focal electric field maximum under the center of the coil where the two loops meet. There has been relatively little information published on the spatial variation of the induced electric fields produced by fo8 coil with bending wings which potentially improves the focality further.

This work presents numerical simulation of transcranial magnetic stimulation by employing fo8 coil with bending wings. Various fo8 coils with different bending angles were numerically designed. Realistic head model obtained from Brooks Air Force Laboratory was employed in this study. The pulse currents with amplitude of 7.7 kA and working frequency 3.6 kHz was fed into the coils. The electrical properties of head tissues are modeled using the 4-Cole-Cole method. The induced electric fields are calculated using the impedance method. Results were compared with those obtained from standard fo8 coil. Results show that either stimulation depth or focality can be well adjusted by changing the bending angle of coil wings. The fo8 coil with flexible folding wings can be served for providing controllable stimulation depth and focality in TMS applications.

P3-101
PRESTIMULUS ALPHA PHASE IN THE SOMATOSENSORY CORTEX INFLUENCES TEMPORAL PERCEPTUAL DISCRIMINATION OF TACTILE STIMULI

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Recent studies demonstrated that prestimulus oscillatory activity can account for perceptual variability despite physically identical stimuli (e.g. Lange et al., 2012). Specifically, the phase of alpha oscillations has been shown to influence visual perceptual performance (e.g. Busch et al., 2009, Mathewson et al., 2009). Here, we tested whether prestimulus alpha phase influences the temporal perceptual discrimination of tactile stimuli.

Neuromagnetic brain activity was recorded with a 306 channel MEG while 16 subjects received two supra-threshold electrical pulses, applied to the left index finger with varying stimulus onset asynchronies (SOAs). Subjects reported if they perceived the stimuli as one or two stimuli. Individual SOAs were determined for which subjects reported to perceive one stimulus in ~50% of the trials. Data were offline analyzed using FieldTrip (Oostenveld et al., 2011) and the circular statistics toolbox for Matlab (Berens, 2009). Virtual sensors in S1 contralateral to stimulation side were generated using linear constrained minimum variance beamformer reconstructions. Alpha phase

angle was computed for each trial by means of a Hilbert transform of single-trial data. Next, we sorted trials with respect to subjects' perception (one versus two) and tested whether phase angles differed between conditions.

Analysis of phase revealed that the angle of alpha-band oscillations significantly differed between conditions in the prestimulus period (-450 ms to -150 ms). No significant differences were found in the poststimulus period.

The results demonstrate that prestimulus alpha phase in S1 determines temporal perceptual discrimination of tactile stimuli. In addition to previous studies (e.g. Busch et al., 2009, Mathewson et al., 2009), we show that oscillatory phase not only influences if a stimulus is perceived or not, but also the temporal resolution of perception. This suggests that the temporal resolution of tactile perception depends on the phase angle of oscillations in the alpha-band during the prestimulus period.

P3-102

CORTICAL GAMMA BAND OSCILLATIONS DURING SOMATIC AND VISCERAL PAIN

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Biomarkers that could allow some objective evaluation of pain perception would have important physiological and clinical implications.

Recently, several studies have implicated gamma band oscillations (GBO) within the somatosensory system as a correlate of pain perception, whilst others have characterised GBO arising from SI following non-painful stimuli.

A key difference between these studies have relates to the differences in stimuli, with laser stimulation selectively activating Aδ and C-fibres whereas transcutaneous electrical stimulation co-activates myelinated sensory Aβ fibres along with nociceptive Aδ and C-fibres.

To explore the relationship between GBO and activation of Aβ and Aδ/C-fibres, participants received painful somatic transcutaneous stimulation and painful electrical stimulation of the Aδ/C-fibre innervated distal oesophagus.

This study shows for the first time that the predominantly A-delta/ C-fibre mediated distal oesophagus can yield gamma band activity in opercular-insular cortex following painful stimuli. Gamma band activity occurred at a similar latency to that observed in those cortical structures following painful somatic stimuli. It would therefore appear that the lack of gamma band activity in the operculo-insular cortex following laser stimulation in earlier studies cannot be entirely attributed to the fact that only A-delta/C-fibres are activated.

P3-103

SOMATOSENSORY PLASTICITY REVEALED BY NEUROMAGNETIC BETA AND GAMMA OSCILLATIONS: EFFECTS OF TRAINING AND PASSIVE STIMULATION

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Recent evidence suggests that extensive training leads to functional improvement even years after a stroke. Furthermore, extensive training may delay the trajectory of aging-related decline in sensorimotor function. Previous studies showed that tactile acuity improves after a short-term passive rhythmic sensory stimulation (RSS) at about 20-Hz (beta band). Our studies aimed to investigate if behavioural changes during training and RSS are accompanied by changes in gamma oscillations because those had been associated with perception and object representation. We investigated changes in neuromagnetic somatosensory beta and gamma oscillations in response to training, as well as experiencing short-term passive vibrotactile stimulation.

We applied 20-Hz vibrotactile stimuli to fingers, recorded somatosensory evoked steady-state beta and gamma oscillations with magnetoencephalography (MEG), and analyzed the underlying cortical source activity using phase coherence in beta and gamma oscillations as the outcome measure.

In the first study, we investigated the effect of music-support training on synchronization of beta and gamma oscillation and their sources in healthy older adults and a stroke patient. An anterior shift of dipole sources and increases in gamma synchrony were found after music training. The increase in gamma synchronization after training can be thought as increased sensorimotor processing, leading toward enhanced somatosensory perception.

In the second study, we investigated changes in somatosensory processing indicated by stimulus-induced beta and gamma oscillations over the time course of an MEG recording session and between subsequent sessions. Beta responses decreased within a session, but recovered after a break between two sessions. In contrast, gamma responses were consistent across repeated blocks and increased between the sessions. The finding that response adaptation occurred only in the 20-Hz beta response, whereas gamma responses showed neuroplastic increases between subsequent sessions suggests that stimulus experience enhances the temporal precision of cortical representation rather than the magnitude of the primary somatosensory response.

P3-104

OSCILLATORY ACTIVITY IN THE SOMATOSENSORY CORTICES PREDICTS THE MOTOR PERFORMANCE OF CHILDREN WITH CEREBRAL PALSY

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The perinatal brain injuries seen in children with cerebral palsy (CP) can result in a wide breadth of sensorimotor presentations that affect the child's mobility and motor control. It has been largely presumed that these motor impairments are primarily a result of abnormal activity within the primary motor cortices. However, outcomes from a few recent neuroimaging studies (e.g., fMRI, DTI, MEG) have begun to challenge this notion by showing aberrant activity in the somatosensory cortices and reduced integrity of the thalamocortical tracts in children with CP. This has resulted in a broad paradigm shift that recognizes the sensory impairments as more central to the aberrant motor performance of these children. In this investigation, we explored the relationship between neural activity in sensory processing networks and the motor impairments seen in children with CP. High-density magnetoencephalography (MEG) and beamforming methods were used to quantify the 4-14 Hz event-related oscillatory changes in the sensorimotor cortices following tactile stimulation to the bottom of the foot in a group of children with CP and age-matched controls. In addition, we measured the ankle plantarflexion muscular strength and gait spatiotemporal kinematics. Our results showed that the children with CP exhibited desynchronization in the medial wall of the contralateral postcentral gyrus ($P < 0.05$, cluster-corrected), whereas the controls had strong synchronization of neuronal discharges in this same brain area ($P < 0.05$, cluster-corrected). In addition, the amount of synchronization within the somatosensory cortices of the children with CP had a strong positive relationship with the strength of the ankle plantarflexor muscles (rho = 0.61; P=0.02), walking speed (rho = 0.68; P = 0.01), and the step length (rho = 0.63; P = 0.01). These results are the first to directly link the motor performance of children with CP with neural activity within the somatosensory processing networks.

P3-105

DISINHIBITION OF THE PRIMARY SOMATOSENSORY CORTEX IS ASSOCIATED WITH CLINICAL PAIN SEVERITY IN PATIENTS WITH FIBROMYALGIA

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Fibromyalgia (FM) is a chronic pain syndrome characterized by the widespread pain and multiple tender points. The present study aimed to investigate intracortical inhibition of the primary somatosensory cortex (S1) in patients with FM, as measured by paired-pulse suppression (PPS) ratio of the N20m–P35m response, by utilizing paired-pulse median nerve stimulation and magnetoencephalography. Since, it has been suggested that the each N20m and P35m component largely represents excitatory and inhibitory postsynaptic potentials at S1, we additionally examined PPS ratios separately for each of these components. The study was comprised of 17 right-handed females with FM and 21 healthy, right-handed females with similar age and education as control group. The median nerve was stimulated at the left and right wrist in separate blocks. Single-pulse stimuli and paired-pulse stimuli with a 100-ms inter-pulse-interval were delivered alternatingly. The cortical responses were modeled with equivalent current dipoles in the contralateral S1. PPS was calculated as the ratio of the amplitudes (peak-to-peak amplitudes of the N20m–P35m, and peak amplitude of the separate N20m and P35m components) between the second and the first responses. The PPS ratio for N20m–P35m in the left(p=0.022) and right(p=0.038) hemispheres were higher in patients with FM than in HC subjects. Notably, PPS ratio for N20m was not different between groups in both the left(p=0.819) and right(p=0.984) hemispheres, whereas PPS ratio for P35m was higher in patients with FM than in HC subject in both the left(p=0.013) and right(p=0.035) hemispheres. Higher PPS ratio for N20m–P35m(r^2=0.354, p=0.012) and for the P35m component(r^2=0.414, p=0.005) in the left hemisphere was positively associated with clinical pain severity (Short-Form McGill Pain Questionnaire, total score). We suggest that bilaterally reduced intracortical inhibition in the S1, probably mediated by a dysfunction in inhibitory postsynaptic potentials, may be a neural correlate of clinical pain in patients with FM.

P3-106

DO BLIND SUBJECTS USE VISUAL AREAS TO PROCESS SENSORY STIMULI?

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We recorded MEG signal elicited by median nerve stimulation (MNS) from two blind and three normal subjects. The stimulation was delivered at three levels, below sensory (sub), just above sensory (supra) and just above motor threshold (motor). Millisecond by millisecond tomographic estimates of activity were extracted from both average and single trial MEG data of each subject. The resulting volume of data was further analyzed in the time and frequency domains. The time domain analysis identified the early (~20 ms post-stimulus) responses to MNS in the primary sensorimotor areas; these

early responses were prominent only for the motor-level stimulation and were similar for blind and sighted subjects. Intermittent and labile changes in activity were also observed, some specifically in the visual areas. The frequency analysis revealed gamma band activity in all comparisons between MNS at the motor and the corresponding supra- and sub-threshold stimulation levels, and substantially more pronounced in the visual areas of blind than sighted subjects. This is in line with claims for higher sensitivity to somatosensory stimuli in blind subjects. We further used mutual information (MI) analysis to identify linked activity between regional activations. This analysis showed no linked activity leading from the somatosensory to the visual cortex for sighted subjects. For blind subjects, the same MI analysis identified stimulus evoked responses linked in a feed-forward way, from the early somatosensory (20-30 ms) to the visual cortex (60-70 ms) through posterior parietal cortex (40-50 ms) [1]. Additional analysis of the data from sighted subjects provided hints for the early part of this feed-forward pathway, but with the activation in the visual cortex inhibited, possibly from sub-cortical input.

[1] AA Ioannides et al. Frontiers in Human Neuroscience 2013;7:429.

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P3-107

MODELING MAGNETIC FIELDS OF EVOKED RESPONSES DUE TO REPEATED SENSORY STIMULATION USING DYNAMICAL CAUSAL MODELING OF INTER-LAMINAR SYNAPTIC CONNECTIONS

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A neural mass model embodying short-term synaptic plasticity and laminar-dependent connections between neural populations has a potential to investigate functional organization of brain regions. Recent Alzheimer Disease (AD) research in animal study Busch et al. 2008 suggested that amyloid plaques may cause hyperactivity in brain. A specialized local cortical circuit model (LCCM) (Wang & Knösche 2013) was fitted to magnetoencephalography (MEG) data to investigate the synaptic connectivity changes in somatosensory cortex.

The left median nerves of the participants were repeatedly stimulated at the wrist using an intensity of 1.3 times above the motor threshold with randomly selected inter-stimuli-intervals (ISI = 30, 60, 90, 120, 150 ms) and 150 repetitions each.

Somatosensory cortex activity was modeled by the first SVD component of a regional source in the primary somatosensory cortex. LCCM model parameters were fitted to this activity of condition ISI120 using Bayesian's inference. Data of eight volunteers were analyzed: 4 healthy elderly, 4 elderly patients: 3 of AD, 1 of mild cognitive impairment). Connection strength varied with presynaptic activity.

The goodness of fit for condition ISI120 in both groups was larger than 95%. The goodness of prediction for conditions ISI90 & ISI150 was larger than 82% in both groups. Three kinds of parameters were further analyzed for all connections (one-way ANOVAs): the connection strength, the rate of plasticity and the synaptic time constant. Just one connection strength was found to differ significantly between groups: the connection from the superficial inhibitory interneurons to deep pyramidal cells: (healthy elderly: 118+140; patient: 2240+990, $p<0.001$, Bonferroni corrected.)

It was found that the patient group shows a stronger inter-laminar inhibitory connection from superficial (Layer 2/3) to deep (layer4/5) cortical layers. This synaptic structure change can be interpreted as a compensatory reaction to the hyperactivity caused by amyloid plaques in AD patients.

P3-108

EFFECTIVE CONNECTIVITY AMONG BRAIN GENERATORS OF SOMATOSENSORY EVOKED HIGH FREQUENCY OSCILLATIONS

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Electrical stimulation of the median nerve elicits a high frequency oscillatory (HFO) component with a mean frequency of ~600 Hz superimposed on the low-frequency primary cortical response of N20. Previous work (Haueisen et al., 2001) has indicated that this HFO activity consists of two distinct components, one that coincides with the ascending slope of N20 and a second one that coincides with the ascending slope of P25. Our aim is to identify and localize the underlying generators of HFOs and determine the information flow among them. Electrical stimulation of the median nerve was performed in 14 healthy individuals. Somatosensory evoked fields (SEFs) of high signal-to-noise ratio (SNR) (3,000 trials) were computed by averaging all artifact free trials. To isolate HFO activity, the MEG signals were band-pass filtered in the 450-750 Hz frequency band. HFO activity was identified in all subjects as a burst superimposed on the low-frequency SEFs components. In all participants, three high frequency components were identified at 18.48±0.79 ms, 21.02±0.611 ms and 25.81±1.61 ms contralateral to the stimulated hemisphere. In five participants, a HFO component was also identified at 54.48±8.09 ms after the stimulus onset. Equivalent current dipoles (ECD) were used to model the underlying HFO generators. The anatomical correspondence of the focus of activity was identified by using cytoarchitectonic maps. The generators of the three HFO components were localized predominantly in Brodmann areas 3b (BA3b), area 2 (BA2), and area 4 (BA4). Effective connectivity among these generators was measured using bivariate Granger causality. Among the three subjects we analyzed so far, we observed a Granger causal influence from the generators in BA3b

to BA2 by a factor of 2.22±1.54. Our study indicates for the first time that multiple functionally connected HFO generators underlie the spatiotemporal integration of incoming sensory information in healthy human brain.

P3-109

MOTOR-RELATED BETA OSCILLATORY RESPONSES LINEARLY INCREASE WITH THE TIME OF DAY

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Previous electrophysiological investigations have evaluated movement-related beta (14-28 Hz) oscillatory activity in healthy participants. These studies have described an abrupt decrease in beta activity that starts before movement onset and a sharp increase in beta power that peaks after movement termination. These oscillatory responses have been respectively termed the beta event-related desynchronization (ERD) or pre-movement beta ERD, and the post-movement beta rebound (PMBR). Previous studies have shown that a variety of movement parameters and demographic factors (e.g., age) modulate the amplitude of these responses, and in the current study we evaluated whether the amplitudes follow a biological temporal rhythm (e.g., circadian), as it is known that spontaneous beta levels increase from morning to afternoon in some brain areas. To this end, we used magnetoencephalography (MEG) to evaluate oscillatory activity during a right hand finger-tapping task in four participants who were recorded at three different times (09:00, 12:00, 16:00) on three consecutive days (i.e., 36 total MEG sessions). All MEG data was corrected for head motion and examined in the time-frequency domain using beamforming methods. We found a significant linear increase in beta ERD amplitude from 09:00 to 16:00 hours in the left precentral gyrus, left premotor cortices, left supplementary motor area (SMA), and the right precentral and postcentral gyri. In contrast, the amplitude of the PMBR was very steady across the day in all brain regions except the left SMA, which exhibited a linear increase from morning to afternoon. Beta levels during the baseline period also increased from 09:00 to 16:00 in most cortical motor network regions. These data show that the pre-movement beta ERD and spontaneous beta levels strongly increase from morning to afternoon, which may indicate that oscillatory beta activity has to be suppressed to a specific threshold in the motor cortices before movements can be executed.

P4-001

FETAL MCG SIGNAL PROCESSING FOR MULTICHANNEL DATA FROM AN ARRAY OF OPTI-CALLY-PUMPED MAGNETOMETERS

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Optically pumped magnetometers (OPM) for the measurement of weak magnetic fields in the femtotesla range have been developed in the last decade. Applications such as magnetocardiography (MCG) and magnetoencephalography with individual or a few channels have been realised. Here the measurement and processing of fetal (f) MCG with an array of 25 microfabricated (m) OPMs will be described.

Individual sensors of 1 cm2 footprint were inserted into three flexible belts containing rigid holders. Two belts were placed on the abdomen and the third on the chest of a pregnant women during the 32nd week of gestation. Raw data show both fMCG and maternal (m) MCG R peaks in appropriate channels.

To improve the fMCG data the mMCG was removed from the multichannel data using an orthogonal projection method based on an estimate of the spatial pattern of the mMCG. Then the fetal heart rate (FHR) was determined from the fetal R peaks found by a Hilbert transform based method. The FHR shows typical variations with a mean heart rate of 150 bpm. As a second method to separate fMCG from the mMCG independent component analysis (ICA) was applied. A resulting fMCG map is dipolar over the abdomen as expected for the fetal heart, the mMCG map shows an increasing field strength towards the chest.

Clearly, the signal processing methods developed for SQUID systems allow easy parameter extraction from multichannel mOPM data. The practical advantages of mOPMs such as room temperature operation and flexible geometry can be exploited without restrictions as exemplified here for fMCG.

P4-002

THE ROLE OF MAGNETOCARDIOGRAPHY IN THE CLINICAL ALGORITHM OF CHRONIC CAD DIAGNOSIS

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Introduction: Coronary artery disease (CAD) in recent decades became a pandemic. According to estimates by WHO mortality from CAD in 2030 will reach 23.4 million people. Therefore, timely diagnosis of CAD is one of the most important tasks of modern cardiology.

Despite the large number of diagnostic alternatives, there remains a need for an inexpensive , accessible and completely safe method with a sufficiently high diagnostic accuracy.

Methods and Materials: Magnetocardiography (MCG) - a non-invasive method for the registration and analysis of the magnetic field generated by the electrical activity of the myocardium - is especially promising from this point of view. In recent years, convincing evidence of high diagnostic efficacy of MCG in diagnosis of CAD was collected. Diagnostic process of heart diseases is nowadays highly formalized and presented in the form of clinical pathways - sequence of clinical decisions, consisting of several levels.

Results: There are several algorithms for diagnosis of CAD based on pretest probability of disease, for example guidance “Chest pain of resent onset” (NICE, UK). The pretest probability is expressed as a percentage. Diagnostic algorithm includes 3 steps. Diagnostic search begins with determining the

calcium score, followed by non-invasive imaging tests (stress- EchoCG , myocardial scintigraphy or SPECT , MRI). Finally, if non-invasive diagnostic methods leave room for doubt, invasive coronary angiography is recommended. We suggest that a MCG test should be an alternative to the calcium score (pretest probability is 10-29 %), or to non-invasive imaging testing (if pretest probability is more then 29 %).

Conclusion: The inclusion of a MCG test as a chronic CAD diagnostic algorithm is feasible from the standpoint of cost/effect and will contribute to the early detection and timely treatment of this most common and dangerous heart disease.

P4-003

DETECTION OF VENTRICULAR TORSION STUDIED WITH MCG CURRENT SOURCE RECONSTRUCTION

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Previous studies reported that ventricular systolic torsion exists in every cardiac cycle, but there is no quantitative analysis gold standard.

Magnetocardiography (MCG) measures magnetic fields at the body surface, which are generated by cardiac electric current sources. These sources can be imaged noninvasively using current source reconstruction (CSR). Some equivalent CSR methods have been reported in bioelectromagnetic research. In 2013, Lu Bing et al. proposed a fast greedy sparse (FGS) method for CSR in MCG. The average goodness of fit of the measured magnetic field map and the map generated by the reconstructed current sources during the QRS complex and ST-T segment were 99.4% and 99.8%, respectively.

In this study, we calculated the source parameters by the FGS method, i.e. source position in the heart and source moment in x and y direction. The continuity of the position curves of reconstructed dominant current sources (strength 65% of the maximal source strength in every moment) were analyzed for the detection of the cardiac torsion moments.

We examined the 61-channel MCG data of 39 healthy subjects and 15 CAD patients. The results showed that source trajectories of 35 healthy subjects and 14 CAD patients displayed at least two position changes in x (or y) direction during QRS complex, where the time interval between the two obvious position changes of the 33 healthy subjects was 12 to 35ms; for the 10 CAD patients it was 16 to 46 ms. 26 healthy subjects had position changes between 41 and 61ms after the beginning of the QRS complex, and for the 10 CAD patients we found 48 to 64ms. In ST-T segment, source trajectories of 10 healthy subjects and 8 CAD patients had one or more position changes.

In summary, the quantitative information of individual left ventricular torsion detected by using this method will be tested and verified further with more subjects.

P4-004

COMPONENT SELECT METHOD IN NOISE REJECTION METHOD USING INDEPENDENT COMPONENT ANALYSIS FOR MCGS

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We studied a method of environmental magnetic noise rejection using Independent Component Analysis (ICA) for Magnetocardiograms (MCGs). ICA is a useful method of separating the signals (MCGs) and the noise. However it is necessary to distinguish between noise components and MCG components from independent components separated by ICA. In many cases, the component selection was determined by a judgment based on viewing. But this method has some problems, such as automatic selection, specific signals by heart disease and variation between individuals.

In order to solve these problems, we proposed a component selection method of distinguishing quantitatively and automatically. This method uses autocorrelation function of electrocardiograms (ECGs) which are simultaneously measured and separated components by ICA. But this method has a problem that measuring ECGs is a source of noise.

We proposed the component selection method without ECGs of distinguishing quantitatively and automatically. The proposed method gave the same results as the method which uses ECGs.

P4-005

A FOUR-CHANNEL HTC RF SQUID TO ANALYZE THE CURRENT PROPAGATION OF THE CARDIAC MAGNETIC FIELD

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We have developed a four-channel high temperature radio-frequency superconducting quantum interference device (HTc rf SQUID) for magnetocardiography (MCG) recordings of heart activity inside a magnetically shielded room (MSR). To achieve the high-quality MCG signal, we explore the new design of the first-order adaptive SQUID software gradiometer technology with a baseline of 80mm, which can adjust its performance timely with the surrounding conditions. The magnetic field sensitivity of each channel is less than 100fT/ÖHz in the white noise region. Especially, in the visualization of MCG signal data, we proposed the curl method not the popular Hosaka-Cohen (HC) transformations, and current density maps (CDM) of P wave, QRS complex, ST segment and T wave were clearly visualized. Simultaneously, we successfully observed the time-varying behavior of the current propagation and estimated the underlying currents. According to these measured results, it is believed that our four-channel HTc rf SQUID magnetometer based on biomagnetic system is available to detect MCG signals with sufficient noise-to-signal ratio. From the characteristics

of current propagation, our CDM is not only a 2D-representation of a 3D-current distribution, but also could reflect the real current density with very high spacial resolution, so it's a potential and promising tool for detecting cardiac microscopic movement mechanism.

P4-006

OPTIMAL CONFIGURATION OF CIRCULAR MARKER COIL FOR MAGNETOCARDIOGRAPHIC IMAGE COMPOSITION

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To achieve highly accurate superimposition (below 2-3mm) of the 3-D cardiac electrical current distribution image obtained from magnetocardiographic (MCG) analysis onto the anatomical heart image, we evaluated the optimal configuration of the circular marker coil.

To make a formula of the magnetic field generated from a circular marker coil on the chest, we used the Neumann's formula. The axes of the circular marker coil were the single (z axis) and triple (x, y and z axis), and diameters of the circular marker coil were 2, 4 and 8 mm. The calculation points of the magnetic field were laid out in an 8×8 (175×175mm) matrix and located on the xy plane at z = 0 mm. We calculated the magnetic field generated from these marker coils at the different position (x and y) and depth (z). We estimated the 3-D position (x, y, z) of the marker coil from the calculated magnetic field by using the Nelder-Mead simplex method. Furthermore, we evaluated the errors of the estimated 3-D position of the each marker coil.

In simulation results, the maximal position errors of the triaxial marker coil for 2, 4 and 8 mm coil diameter were almost same. In particular, the maximal position error of the triaxial marker coil (depth from the marker coil to the calculation point ≦ 40 mm) was below 3 mm. In contrast, the maximal position errors of the single-axis marker coil were about 10-20 mm.

We concluded that the triaxial marker coil (diameter: 2-8 mm) is suitable for the high-accuracy MCG image composition.

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P4-007

FETAL MAGNETOCARDIOGRAPHY WITH ATOMIC MAGNETOMETER ARRAY

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We have developed an array of optically pumped atomic magnetometers for use in fetal magneto-cardiography (fMCG). It comprises four 87-Rubidium atomic magnetometers operating in the Spin-Exchange Relaxation Free (SERF) regime [1,2]. With a sensitivity of 5 fT/rHz, the magnetometers have been used for fMCG on fetuses with gestational ages as young as 20 weeks. One important effect in operating an array of optically pumped magnetometers is the vector AC Stark shift. This generates an effective magnetic field in the atomic vapor that can complicate the operation of an array--serving as an additional source of noise. We will describe our efforts to limit the Stark shift induced magnetic field [3] along with other developments towards having a robust, reliable and sensitive array of atomic magnetometers.

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P4-008

MAGNETOCARDIOGRAPHY CAPABILITIES IN MYOCARDIUM INJURIES DETECTION

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Aims: Objective of this research was the investigation of MCG capabilities in diagnosis of ischemic and inflammatory myocardial injuries using new MCG markers of the spatiotemporal organization of myocardium excitation.

Methods: 128 patients were examined: 1st group were 34 healthy volunteers; 2nd group - 62 IHD pts with and without acute ST-segment elevation myocardial infarction; group 3 included 32 pts - with acute myocarditis. MCG-mapping was performed at rest on the 7-channel MCG-scanners "Cardiomagscan" V 3.1 (Company KMG, Ukraine) in non-shielded MCG laboratory. 11 MCG parameters for selected time intervals of the cardiac cycle were tested : QRS duration; Delta 80 - maximum current density (CD) vector deviation at 80 ms from the J-point; D1; D2; D3; D4 - maximum CD vector deviation at 4 ST-T sub-intervals (starting at 60 ms from the J-point); Ta-e - time interval duration from the peak to the end of T-wave; Delta RT - difference between direction of the maximum CD vector at R and T peaks; SumR/SumT - ratio of the global CD at the R-peak to the global CD at the T-peak; MaxR/MaxT - ratio of the maximum CD at the R-peak to the maximum CD at the T-peak; (QRS- t1)/t1 - symmetry factor of the QRS complex.

Results: In AMI pts values of MCG parameters were higher than those in patients with stable IHD or myocarditis and healthy subjects. 2nd and 3rd groups differed from healthy patients by 8 of 11 markers. Application of discriminatory analysis allowed us to get classification functions, which could be used (with 82 % accuracy) to qualify just examined patient to the investigated categories.

Conclusion: New MCG markers are useful for detection of myocardial abnormalities of ischemic and inflammatory origin with high sensitivity and specificity.

Keywords: electric heterogeneity, magnetocardiography, myocardial ischemia, myocarditis, differential diagnostics

P4-009
CHARACTERIZING PROPERTIES OF MEG AND EEG SIGNALS GENERATED BY EXTENDED SOURCES

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The sensitivity patterns of magnetoencephalography (MEG) and electroencephalography (EEG) sensor arrays have complementary properties in terms of the orientation and the depth of focal source elements. For extended source patches on the folded cortical surface, MEG and EEG signals generated by source elements on opposing sulcal walls will partially cancel out. This selective cancellation of source components of certain orientation is expected to result in systematic differences in MEG and EEG. To quantify this effect, we defined a radiality index based on the source orientation of least MEG sensitivity at each location within a patch. The index is a measure of the relative contribution of approximately radial and tangential source components to the MEG and EEG data. Maps of the radiality index for simulated source patches suggested that, for a large proportion of lateral and dorsal cortical regions, the main contribution from extended sources to the EEG signal is expected to come from the MEG-insensitive radial source components, whereas for medial and ventral regions the main contribution is expected from tangential components. The selective cancellation of signals from source components of specific orientation within extended source patches contributes to the complementarity of MEG and EEG.

P4-010
ASSESSMENT OF SUBCORTICAL SOURCE LOCALIZATION USING DEEP BRAIN ACTIVITY IMAGING MODEL WITH MINIMUM NORM OPERATORS: A MEG STUDY

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Subcortical structures are involved in many healthy and pathological brain processes. It is crucial for many studies to use magnetoencephalography (MEG) to assess the ability to detect subcortical generators. Another crucial point is the ability to perform useful directed connectivity measures between the cortex and these areas. This study aims to assess

1. the source localization accuracy and to compare the characteristics of three inverse operators in the specific case of subcortical generators.
2. the possibility the detect causal relationship between cortical and subcortical areas of interest in a resting-state paradigm.

MEG has a low sensitivity to subcortical sources mainly because of their distance from sensors and their complex cyto-architecture. However, we show that using a realistic anatomical and electrophysiological model of deep brain activity (DBA), the sources make measurable contributions to MEG sensors signals. Furthermore, we study the point-spread and cross-talk functions of the wMNE, sLORETA and dSPM inverse operators to characterize distortions in cortical and subcortical regions and to study how noise-normalization methods can improve or bias accuracy. We then run Monte Carlo simulations with neocortical and subcortical activations. In the case of single hippocampus patch activations, the results indicate that MEG can indeed localize the generators in the head and the body of the hippocampus with good accuracy. We then tackle the question of simultaneous cortical and subcortical activations. wMNE can detect hippocampal activations that are embedded in cortical activations that have less than double their amplitude, but it does not completely correct the bias to more superficial sources. dSPM and sLORETA can still detect hippocampal activity above this threshold, but such detection might include the creation of ghost deeper sources. Finally, using the DBA model, we showed that the detection of weak thalamic causal loops of ongoing brain activity is possible.

P4-011
SIMULTANEOUS RECORDING OF INTRACEREBRAL STEREOTAXIC EEG, SCALP EEG AND MEG IN EPILEPSY

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Introduction: Magnetoencephalography (MEG), scalp electroencephalography (EEG) and intracerebral stereotaxic EEG (SEEG) are measures used for pre-surgical evaluation of intractable epilepsy. While the signals recorded in the three modalities capture the same type of neural activity, the relationship between surface and depth recordings is largely unresolved. An ideal approach for addressing this issue is to perform simultaneous recordings of MEG, EEG and SEEG. Here we present two patients for whom we performed such recordings.

Method: Two patients with intractable epilepsy underwent an SEEG implantation for presurgical evaluation. At the end of the evaluation, EEG electrodes were placed on the patients' scalp. Data were then acquired on a 4D Neuroimaging MEG system. Care was taken to minimize artefacts on the MEG traces. Interictal spikes were marked on the SEEG, and average signals on MEG and EEG were obtained based on these triggers.

Results: For the first patient, the averaged signals of MEG and SEEG had similar spike morphologies. Source localization indicates a region that is consistent with planned surgery. For the second patient, a clear slow wave was visible at the surface, whereas the initial wave identified with SEEG was not seen.

Conclusion: We show that we can obtain averaged signals of good quality on MEG and EEG simultaneously with intracerebral EEG. Correspondence between SEEG and surface is not one-to-one, which opens a number of perspectives for exploring the detectability of signals at the surface given the depth source configuration.

P4-012

WHERE IS THE HEAD? ACCOUNTING FOR HEAD LOCATION UNCERTAINTY INSIDE THE MEG HELMET

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MEG brain imaging has become a popular technique for obtaining brain images with high temporal resolution. However, precise estimates of neuronal current flow are undermined by uncertain knowledge of the head location with respect to the MEG sensors. This is mostly caused by undetected head movements or poor placement of fiducials. Previous studies have demonstrated that the inverse solution may be severely affected by the typical co-registration error of 5-10 mm (Hillebrand and Barnes, 2011); indeed, a small rotation of the head may generate a completely different brain image (López et al., 2012). In recent work we presented a methodology for determining the correct location of the brain based solely on MEG data (López et al., 2012). We used a Metropolis search followed by Bayesian Model Averaging over multiple sparse prior source inversions with different head location/orientation parameters, in order to provide a posterior distribution over head location. In this approach the negative variational free energy was used for model selection with encouraging results. I will show how we have been able to validate this method using subject-specific head-casts (Troebinger et al., 2013) in which the true anatomical location is known. I will also discuss other possible ways of minimising or marginalising out co-registration error from MEG data.

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P4-013

USING DIFFUSION MRI INFORMATION IN THE MAXIMUM ENTROPY ON MEAN FRAMEWORK TO SOLVE MEG/EEG INVERSE PROBLEM

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Magnetoencephalography (MEG) and Electroencephalography (EEG) inverse problem is well-known to require regularization in order to avoid ill-posedness. Usually, regularization is based on mathematical criteria (minum norm, ...). Physiologically, the brain is organized in functional parcels and imposing a certain homogeneity of the activity within these parcels was proven to be an efficient way to analyze the MEG/EEG data [1]. The parcels of information can be computed from diffusion Magnetic Resonance Imaging (dMRI) by grouping together source positions shared by the same connectivity profile (computed as tractograms from diffusion images).

In this work, three parcel-based inverse problem approaches have been tested. The first two approaches are based on minimum norm with added regularization terms to account for the parcel information. They differ by the use of a hard/soft constraint in the way they impose that the activity is constant within each parcel [4]. The third approach is based on the Maximum Entropy on Mean (MEM) framework [2]. It models source activity with a random variable and parcels are also used as a regularization. Several tests have been conducted with synthetic and real data[3] that encompass the MEG/EEG and the diffusion magnetic resonance signals to compare these three approaches in terms of active region-detection accuracy.

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P4-014

BAYESIAN SOURCE MODELING OF MEG DATA FOR CEREBELLAR ACTIVITY ASSESSMENT

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It is a matter of debate whether scalp recordings with EEG and MEG can be used to infer information on the functional role of the cerebellum. There are indeed technical and practical reasons that make the cerebellum less "visible" with these techniques, but there are also reasonable expectations that a thorough data analysis can highlight activity in this part of the brain.

Here we describe the analysis of MEG data recorded at the MEG Center at the University Hospital Tübingen, Germany, with a 275-channel whole-head MEG-system. The data consist in the recording of tapping with left or right finger for four subjects. The measurements were averaged thanks to the trigger given by a photoelectric barrier. The analysis is performed in both the time domain and the frequency domain, with the purpose of localizing possible activity both in the cerebellum and in sensorimotor cortex.

A MRI template was used as source space and the cerebellum region was extracted by means of Freesurfer software [1]. Brainstorm software [2] was used to compute the forward problem. Brainstorm was also used to compute distributed spatio-temporal estimates of the brain activity with dSPM and wMNE. Automatic multi-dipole modeling was performed with a Particle Filter (PF) [3] and a Sequential Monte Carlo sampler (SMC) [4]. Analysis in the frequency domain was performed using DICS, as well as the SMC sampler; in particular, since the subjects tapped with a 2-3 Hz frequency, we investigated this frequency window.

Preliminary results with PF and SMC show activation in the cerebellum region. Further investigations will be carried on to assess the reliability of these reconstructions.

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P4-015

COBRA: A NEW APPROACH FOR MRI-CONSTRAINED SOURCE RECONSTRUCTION USING BEAMFORMING TECHNIQUES

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Adaptive beamforming has become a widely used and popular method for source reconstruction in MEG. A major advantage of this approach is the derivation of optimal source parameters from the measured data covariance, which improves both spatial resolution and suppression of interference sources. A disadvantage of this approach, particularly for spatiotemporal imaging, is the loss of source polarity information for specific brain locations. This complicates both averaging of source activity and phase statistics across subjects, and the interpretation of the underlying neural sources, such as modeling extended sources in epilepsy research. This shortcoming can be avoided by using MRI-derived cortical surfaces to disambiguate source orientation, although this requires both accurate surface geometry and minimal co-registration error. We propose a novel approach, dubbed COBRA (Cortically Oriented Beamforming with Recursive Alignment) for cortical surface imaging using event-related minimum-variance beamforming. We will present validation of the method using both data simulations, as well as MEG recordings of visual evoked responses to reversing checkerboard wedges of varying size in adult subjects to simulate the effects of source extent and MRI-MEG co-registration errors. High-resolution cortical surface meshes (81920 vertices per hemisphere) of the white and gray matter and midpoint boundaries were obtained using the CIVET software (Montreal Neurological Institute). We describe methods for improving and correcting co-registration through recursive alignment of the MRI surface to the beamformer derived source orientations, in addition to estimating the effects of co-registration error and head movement. The COBRA algorithm will be incorporated into the BrainWave toolbox freely available to the MEG community through our web site (cheynelab.utoronto.ca/brainwave).

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P4-016

USING MYELIN DENSITY MAPS TO INFORM M/EEG SOURCE RECONSTRUCTION

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A fundamental tenet of neuroscience is that function and structure are tightly linked. We present an approach for combining high resolution MRI-based myelin mapping with electroencephalography (EEG) or magnetoencephalography (MEG).

EEG and MEG signals can be observed on the scalp due to the homogenous alignment and high local connectivity of pyramidal neurons in the cortical sheet generating a macroscopic net signal. Here we make use of the known microstructural variation in pyramidal cell density (and hence current density) both across the cortex and over individuals and link these structural differences with the variation in cortical current density as measured by M/EEG. Recent studies (Sereno 2013, Dick 2012, Lutti 2013) have made it possible to non-invasively measure myelin density throughout the cortex with widely available 3T MR technology. Since pyramidal cell density in the cortex is related to the local myeloarchitecture (Hellwig 1993), we expected that the myelination measures predict functional MEG measures.

We reanalysed data from a previous auditory MEG experiment (Sedley 2012). Pitch onset evoked response fields (ERFs) were source localised by means of a variational Bayesian equivalent current dipole algorithm. The myeloarchitecture was estimated indirectly from individual high-resolution multi-parameter maps (Weiskopf 2013). We were able to show that myelin estimates across cortical areas correlated positively with dipole magnitude across hemispheres. Bayesian regression was used to identify lateral Heschl's gyrus as the most likely origin of the ERFs measured by MEG.

We demonstrated the predictive value of non-invasive myelin maps for the strength of the MEG signal in the auditory cortex, explaining both inter- and intra-individual functional differences by anatomical measures. This work presents a significant step towards exploiting the higher spatial resolution of quantitative multi-parameter maps in order to identify the cortical origin of M/EEG signals, inform M/EEG source reconstruction and explore structure-function relationships in the human brain.

P4-017

A BEAMFORMER FOR SOURCE LOCALIZATION IN ELECTROCORTICOGRAPHY

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ElectroCOrticoGraphy (ECoG) is the gold standard to map focal interictal spiking, and to determine the extent of the resection whenever surgical removals of parts of the brain are necessary. Recording from the inside the brain electrical activity provides a signal with high signal-to-noise, which can be used to validate other non-invasive neurophysiological techniques like magneto- and electroencephalography (MEEG) [1].

In the last few years, some papers have presented methods to solve the ECoG inverse problem [2] of reconstructing the spatio-temporal distribution of the neural currents responsible of the recorded signal.

This study realizes an analysis of the ECoG source modeling problem considering three different aspects. First, we compute the lead-field matrix mapping the neural currents onto the sensors space by applying a new function that we realized within the framework of the OpenMEEG software [3]. Second a systematic study of the numerical stability associated to the ill-posed ECoG inverse problem is performed by analyzing the condition number of the lead-field matrix for several simulated electrode grids characterized by different positions on the brain, different electrode layouts and different numbers of electrodes. Finally, we solve the ECoG inverse problem by applying a Linear Constraint Minimum Variance beamformer [4]. This method is applied to both synthetic data and a set of real measurements recorded while a subject performed a visual categorization task.

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P4-018

INFLUENCE OF THE HEAD MODEL ON EEG AND MEG SOURCE CONNECTIVITY ANALYSIS

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The objective of the present study is to examine the influence of the head model on source connectivity analysis in EEG and MEG.

As a reference, a detailed finite element head model was created, comprising six layers: skin, hard/spongy bone, cerebrospinal fluid (CSF), and white/grey matter. Four test models were derived from that reference model to consider the effects of particular simplifications: ignoring white/grey matter distinction, ignoring hard/spongy bone distinction, not modeling CSF, and reduction to a 3-layer model (skin, skull, and brain). The source space was placed to inside of the grey matter layer with surface normal orientation. For connectivity simulation, we assumed a two-source scenario in which one source is fixed at one position and the other source is sequentially located at all other positions of the source space. Each source time course was simulated by a neural mass model comprising 3 neural populations for pyramidal cells and excitatory/inhibitory interneurons. The connectivity from source 1→2 was realized by coupling the output of the pyramidal cell population in source 1 to the input of the excitatory interneuron population of source 2. An LCMV beamformer was used for source reconstruction, and imaginary coherence (IC) and generalized partial directed coherence (GPDC) were used as connectivity measures. The connectivity results were compared using the relative error between the results of the original signals and that of reconstructed signals.

Our results show that neglecting white/grey matter distinction and CSF more affect the reconstructed source time courses and their connectivity analysis than neglecting hard/spongy bone distinction when an optimized skull conductivity value is used. Large inverse and connectivity errors are found in certain regions showing large topography errors in forward solution. The IC is less affected by the cross talk effect and yields lower and more spatially restricted errors than GPDC.

P4-019

THETA-MEDIATED OSCILLATORY NETWORKS ACTIVATED BY SPATIAL MEMORY AND NAVIGATION REVEALED WITH P-EPISODE DETECTION IN COMBINATION WITH MEG SOURCE RECONSTRUCTION

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The P-episode method is an alternative to other spectral analysis techniques, initially designed for detecting transient oscillatory states in intracranial EEG recordings (Caplan et al., 2001). This method identifies epochs with sustained oscillatory activity, based on duration and amplitude thresholds extracted from a linear fit to the logarithm of the background power spectrum. Here, we adapted and applied the method to magnetoencephalographic (MEG) signals to detect and localize the sources of theta oscillatory episodes. For this purpose, we performed MEG recordings while healthy young adults were engaged in a memory and spatial navigation task implemented in a computer-simulated environment. The task consisted in remembering the direction and location where houses appeared within a circular arena. Visual cues were exclusively distal, including sun, clouds, mountains, and a wall. Participants used a joystick to control their

movements in the arena. We applied the P-episode algorithm to the MEG data, after removing the independent components (IC) corresponding to ocular, muscular, and other artifacts. Additionally, we also identified the P-episodes on the ICs showing the strongest contribution to sensor theta (4-8 Hz) activity. Interestingly, P-episodes were detected more often near 6 Hz in all 8 subjects, and lasted several cycles. To obtain the sources of theta P-episodes, we bandpass filtered (4-8 Hz) and segmented the data in epochs with and without P-episodes. Spatial filters were computed using DICS and BEM models based on individual MRIs. Using a hierarchical model approach, we contrasted the source maps computed for segments with and without P-episodes. This analysis revealed that the main theta sources were localized in cerebellum, calcarine sulcus, medial temporal lobe and medial frontal regions. Validation of these results using intracranial EEG (iEEG) and simultaneous iEEG-MEG recordings is in progress.

P4-020

ANALYSIS OF VISUAL AND AUDITORY CONGRUENCY TESTS USING MIXED NORM EEG SOURCE RECONSTRUCTION WITH PERTURBED SOURCE MODELS

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The field spread observed in electroencephalography (EEG) signals due to the volume conduction in the electrically conducting head makes correct interpretation of source connectivity difficult in sensor space. We present a methodology that uses refined source models in spatially sparse l21 EEG source reconstructions based on mixed norm cost functions and apply this to visual and/or auditory (in)congruent stimuli to uncover the source connectivity between active neural source regions in cognitive control.

The used l21-norm EEG source reconstruction algorithm has a l1-norm (l2-norm) regularization in space (temporal domain). First, we project the measured signals on temporal basis functions which are based on the singular value decomposition of the measurements matrix. For the conditions having highly correlated time varying temporal basis function, a source reconstruction is performed starting from the collected signals projected on those basis functions so to spatially refine the sources. Second, an analysis of the spatial correlation differences as function of time between pairs of conditions is performed. In case of large variations in spatial correlation, a refined time window is defined wherein the perturbed sources are reconstructed so to have more clear contrast between the sources associated to the stimuli.

A 64-channel EEG setup is used, the number of unknowns in the inverse algorithm was 31896 with a spherical head model, 3-6 temporal basis functions were extracted, and we assumed free orientations of the neural dipole sources. Similar temporal variations in the first basis function were observed across stimuli and corrected the associated source space. In the higher order temporal basis functions, incongruency appears, i.e. source reconstructions are spatially uncorrelated in specific time windows, and are corrected. We observed on average a correlation of approximately 60% between congruent auditive and congruent visual, whereas the correlation between congruent auditive (visual) and incongruent auditive (visual) was only 30%.

P4-021

MODELING THE ACTIVE NEURODYNAMICS OF TMS USING REALISTIC NEURAL TRACTS

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In Transcranial Magnetic Stimulation (TMS), an applied dynamic magnetic field induces electric fields in the brain that interact with the neural system by altering membrane potentials. Gaining more insight with TMS modeling is crucial because in vivo measurements are expensive, difficult, and restricted due to ethical issues.

We developed a toolbox that models TMS in a case- and subject-specific way from the macroscopic fields to the potentials on microscopic neuronal level. It directly retrieves its inputs from the TMS neuronavigation system, which monitors the coil position and orientation relative to the subject's head during an experiment. Head models are constructed with realistic geometry, tissue heterogeneity, and anisotropy based on structural and diffusion-weighted MRI (DTI) with ±1-mm resolution. Moreover, neural pathways are traced using DTI-based tractography (Leemans,2009). TMS can induce direct and indirect waves, originating from the stimulation of pyramidal neurons directly or via interneurons, respectively. Therefore, both types are included and modeled as compartmental neurons containing dendrites, soma, axon hillock, Ranvier nodes, and myelinated internodes with passive and active membrane properties as in (Salvador,2009).

First, the induced electric field distribution is computed using a recently developed electromagnetic solver (DeGeeter,2012), which leads to three stimulation mechanisms (Silva,2008). Within a 5-mm range near the maximal field, a group of 100 neural tracts between 5 and 25 cm is selected. Second, the spatio-temporal variation of the membrane potentials is computed along these neurons over a period of 20 ms with a 1-μs time step. It is important to embed realistic tracts since the neuron's orientation is a crucial parameter.

This toolbox can, for example, investigate the sensitivity of coil positioning, predict the mechanism and initial location of excitation and estimate which pathways contribute effectively to the stimulation. Moreover, it can help interpret TMS experiments and their electrophysiological responses recorded with EEG and/or EMG.

P4-022

REAL-TIME SOURCE LOCALIZATION USING MINIMUM NORM ESTIMATION AND REGION OF INTEREST CLUSTERING

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Whereas data analysis to date is mostly done subsequent to the acquisition process, we introduce an approach to monitor distributed brain activity at the source level in real-time. Brain monitoring provides a feedback which e.g. allows real-time adaption of experimental parameters to the subject's reactions and increases time efficiency by shortening acquisition and subsequent offline analysis. In this work we present a clustering method for real-time distributed source localization which is able to handle low SNRs and reduces at the same time the high computational effort.

Our method is based on two assumptions: firstly it is assumed that the neural activity can be organized into functional cortical parcels. Secondly it is assumed that a low SNR reduces the number of distinguishable source localizations. Given these two assumptions, region-wise clusters are calculated based on Destrieux's brain atlas which results in a downsized gain matrix.

A minimum norm estimation (dSPM) is used as real-time source localization algorithm which maps the MEG/EEG measurement to the clustered source space. The localization result is a distributed activity map of brain atlas regions.

Our algorithm is able to handle Elekta Neuromag® VectorView™ 306 channel MEG measurements with a sampling rate of 1250 sps as well as ANT 128 channel EEG measurements with a sampling rate of 2048sps. Studies using human MEG/EEG evoked data show that the proposed real-time technique is accurate and fast using a moving average containing 10 averages. Responses to auditory and somatosensory stimuli are successfully localized.

The reduced number of dipoles and a preserved variance of the gain matrix improve the ability to distinguish active regions and speed up the localization. Online brain monitoring is a useful addition to common acquisition methods and allows to process more information during the measurement.

P4-023

ACCURACY OF A SOURCE ESTIMATION BASED ON MODIFIED L1-NORM MINIMIZATION

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We developed a source estimation method to obtain spatio-temporal neural sources for linguistic MEG data. In this presentation, we are discussing the accuracy of the method on the basis of a realistic simulation, applications of the method to actual linguistic data, and a comparison between the active locations estimated by the method and those detected by fMRI.

Our source estimation method has two-step procedures: estimating major active locations by minimizing modified l1-norm, and estimating strengths of dipole moments at major active locations by a least-squares error. Further, we execute a grouping procedure of taking a vector-sum of moments of inseparable dipoles, and transform the group locations on a standard brain. Empirically, 60-80 major active locations, and 10-30 dipole groups were obtained for linguistic data.

We carried out a realistic simulation in which five neural sources were simultaneously active to explain the N400 component of linguistic activations. The simulated location error had the mean standard deviation (SD) of 4 mm along a coordinate for the five sources when MEG average data had a signal-to-noise ratio of 10. The application of the present method to linguistic experimental data showed that the major active locations included almost of all fMRI active foci, if we neglected ±1 cm difference. The location of dipole group had the mean SD of 9 mm along a coordinate for the five sources and four linguistic experimental data that included about ten subjects each.

The experimental SD in location of the dipole group (9 mm), which included variations between subjects, was consistent with the simulated SD in dipole location (4 mm). Further, the major active locations were considered to be reasonable from previous findings on linguistic activations. These results show that we succeeded in estimating multiple neural sources that were simultaneously activated for linguistic processing.

P4-024

MEG SOURCE RECONSTRUCTION WITH IDENTIFYING DIRECTED SOURCE INTERACTIONS ON STRUCTURAL BRAIN NETWORKS

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In the present study, we propose a new MEG source reconstruction method that simultaneously estimates source amplitudes and interactions over the whole brain. In the proposed method, a full multivariate autoregressive (MAR) model are used for formulating directed interactions (i.e., effective connectivity) between sources. The coefficients of the MAR matrix are constrained by the prior knowledge of whole-brain structural networks inferred from diffusion MRI data, where the MAR coefficients for structurally disconnected source pairs are excluded from the estimation by being set to zero. In addition, we employ an fMRI prior on the spatial activity patterns and a sparse prior on the MAR coefficients to improve the accuracy and robustness of the proposed method.

The observation model of MEG data, the MAR-based dynamic source model, and a series of the prior knowledge are integrated into a Bayesian framework using a state-space representation. To jointly estimate the parameters in the model, such as the source amplitudes and the MAR coefficients, we

adopt the variational Bayesian technique for deriving a tractable and computationally efficient algorithm. The model formulation and the estimation algorithm above allow identifying the effective connectivity across the whole brain, without requiring the selection of regions of interest.

The proposed method is evaluated on simulated and experimental data. Compared with its non-dynamic counterpart, where the source amplitudes and the MAR coefficients are separately estimated in a two-stage manner, the proposed method improves quantitative performance measures in simulations, and provides better physiological interpretation and inter-subject consistency in application to face perception data.

P4-025

REWEIGHTED MIXED-NORM ESTIMATES FOR SPATIO-TEMPORAL MEG/EEG SOURCE RECONSTRUCTION

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Source imaging with magnetoencephalography and electroencephalography allows the noninvasive analysis of the brain activity with high temporal and good spatial resolution. Since the MEG/EEG inverse problem is ill-posed, inverse solvers use a priori knowledge on the sources to find a unique solution. For the analysis of evoked brain signals, constraints promoting spatial sparsity of the sources can be applied. Due to its convexity, l1 norm regularization is often used for this purpose. However, the resulting source estimates are known to be biased in amplitude and often suboptimal in terms of source selection. To overcome this drawback, non-convex regularization functionals based on lp quasinorms with $0 < p < 1$ can be applied. Regularized regression with both lp quasinorm and l1 norm penalties is however only applicable to single measurement vector problems. Therefore, both approaches cannot account for the temporal characteristics of the neural activation.

In this work, we present an MEG/EEG inverse solver, which employs a l2,0.5 quasinorm penalty. As the Mixed Norm Estimate, which is based on a l2,1 mixed-norm penalty, the proposed regularized regression approach promotes spatial sparsity as well as temporal stationarity of the neuronal activation. The resulting non-convex optimization problem is solved with an iterative reweighted scheme using convex surrogate optimization subproblems, which we call the iterative reweighted Mixed Norm Estimate. Each subproblem is solved with a block coordinate descent scheme, a convergence control by means of the dual gap, and an active set strategy. The proposed algorithm allows to compute the iterative reweighted Mixed Norm Estimate on real MEG/EEG inverse problems with and without orientation constraint.

We provide empirical evidence based on simulations and analysis of MEG data that the proposed method outperforms the standard Mixed Norm Estimate in terms of active source identification and amplitude bias.

P4-026

RECONSTRUCTION OF NON-STATIONARY BRAIN ACTIVITY USING SPACE-TIME-FREQUENCY DICTIONARIES

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Functional study of the brain -functional neuroimaging- allows to identify the spatial dynamics of brain responses associated with certain stimuli or diseases. One widely used technique to perform functional neuroimaging are Magneto or Electroencephalographic (M/EEG) signals recorded on the scalp. However, from a mathematical point of view, extracting spatial information from M/EEG recordings -M/EEG inverse problem- is a heavily ill-posed problem. To solve such problems, prior assumptions should be made about brain activity. The proposed approach is based on merging ideas that have been constantly presented in state of art methods, but that have not been used under an unified framework: On the one hand, we assume that brain activity can be represented through a sparse linear combination of spatial basis functions. On the other hand, we assume that time series of estimated brain activity consist of a small set of time-frequency atoms extracted from a given time-frequency representation. Our approach allows to obtain locally smooth, sparse, and highly interpretable solutions in the spatial domain, while the use of well-localized time-frequency atoms allows to relax strong stationarity assumptions that are usually made in some state of art methods. To assess the accuracy of our approach, simulated data was used to objectively compare the spatial and temporal quality of the reconstruction against two state of art methods in which our approach is based: Sparse Basis Field Expansion (S-FLEX) and Time-Frequency Mixed Norm Estimate (TF-MxNE). Simulation results show that the proposed approach achieves a trade off between spatial and temporal accuracy, unlike S-FLEX and TF-MxNE, where a good performance in one of the domains, implies sacrificing performance in the other domain. Finally, the proposed approach was validated using real data. Specifically, our approach succeeded in localizing ERPs of a standard oddball experiment for a Brain Computer Interface task.

P4-027

ANALYSIS OF SPATIAL RESOLUTION AND CROSSTALK OF DIFFERENT DISTRIBUTED SOURCE LOCALIZATION METHODS IN EEG AND MEG.

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The spatial resolution of an EEG or MEG inverse operator is an important feature in the context of distributed source localization when estimating

spatial extent of the underlying generator, or when assessing how functional connectivity patterns could be biased by crosstalk between sources.

We estimated the resolution matrix (Grave de Peralta Menendez et al., Human Brain Mapping, 1997) to evaluate the spatial resolution properties of 4 source localization methods, namely: the minimum norm estimate (MNE) and its noise-normalized extensions (dSPM and sLORETA) as well as the maximum of entropy on the mean (MEM, Chowdhury et al., Plos One 2013) when applied either on high-density EEG (256 electrodes) or MEG data (275 gradiometers). While the resolution matrix of MNE, dSPM and sLORETA was calculated analytically, the resolution matrix of MEM was constructed using Monte-Carlo simulations, since MEM is not a linear operator. We characterized the resolution matrix of each method using measurements of dipole localization error and spatial dispersion, when applied whether on point spread functions (PSF) of crosstalk functions (CTF) (ie rows versus columns of the resolution matrix).

Our results showed that the localization error was similar for all the techniques for PSF and CTF, except for sLORETA providing zero-error for PSF as expected in absence of noise. Besides, MEM showed more accurate results in terms of spatial dispersion in PSF and CTF, when applied either on EEG or MEG data. Globally the spatial error and dispersion was higher in EEG than in MEG.

The study shows that MEM has higher spatial resolution than linear techniques. We planned to validate these results using somatosensory data obtained with electrical median nerve stimulations, as proposed in Molins et al. Neuroimage 2008. The source reconstruction of the inverse operators will be compared to a dipole fit to estimate the localization error and dispersion.

P4-028

MEG SOURCE IMAGING METHOD USING FAST L1 MINIMUM-NORM AND ITS APPLICATIONS TO SIGNALS WITH BRAIN NOISE AND HUMAN RESTING-STATE SOURCE MAGNITUDE IMAGES

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The present study developed a fast MEG source imaging technique based on Fast Vector-based Spatio-Temporal Analysis using a L1-minimum-norm (Fast-VESTAL) and then used the method to obtain the source amplitude images of resting-state magnetoencephalography (MEG) signals for different frequency bands. The Fast-VESTAL technique consists of two steps. First, L1-minimum-norm MEG source images were obtained for the dominant spatial modes of sensor-waveform covariance matrix. Next, accurate source time-courses with millisecond temporal resolution were obtained using an inverse operator constructed from the spatial source images of Step 1. Using simulations, Fast-VESTAL's performance of was assessed for its 1) ability to localize multiple correlated sources; 2) ability to faithfully recover source time-courses; 3) robustness to different SNR conditions including SNR with negative dB levels; 4) capability to handle correlated brain noise; and 5) statistical maps of MEG source images. An objective pre-whitening method was also developed and integrated with Fast-VESTAL to remove correlated brain noise. Fast-VESTAL's performance was then examined in the analysis of human median-nerve MEG responses. The results demonstrated that this method easily distinguished sources in the entire somatosensory network. Next, Fast-VESTAL was applied to obtain the whole-head MEG source-magnitude images from resting-state signals in 41 healthy control subjects, for all standard frequency bands. Comparisons between resting-state MEG sources images and known neurophysiology were provided. Additionally, in simulations and cases with MEG human responses, the results obtained from using conventional beamformer technique were compared with those from Fast-VESTAL, which highlighted the beamformer's problems of signal leaking and distorted source time-courses.

P4-029

TIME SHIFT BETWEEN THE INTERICTAL SPIKES IN SIMULTANEOUS EEG AND MEG RECORDINGS REFLECTS DIFFERENT EPILEPTOGENIC GENERATORS

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Electroencephalography (EEG) and magnetoencephalography (MEG) present different sensitivity profiles for the detection and localization of neuronal activity. It is still unclear how these different profiles affect the interpretation of source localization findings during the presurgical evaluation of epileptic patients.

Here, we aim to define the temporal relationship between interictal spikes recorded simultaneously with EEG and MEG and the relationship between their underlying generators.

EEG and MEG data were simultaneously recorded from a four-year old epilepsy patient with tuberous sclerosis complex (TSC) having a large calcified cortical tuber among others small. We averaged morphologically consistent interictal spikes separately in EEG and MEG signals and estimated their temporal relationship. The peak of the interictal spike occurred in the MEG signal 20 ms before the peak of the interictal spike in the EEG. We localized with equivalent current dipoles (ECD) the activity from the onset of the early MEG spike to the endpoint of the later EEG spike. We further reconstructed the minimum norm estimates (MNEs) to the peak latency of the averaged spike.

ECD traces localized to the averaged spikes in EEG and MEG circumscribed the large calcified cortical tuber in its millimeter vicinity. The ECD trace localized to the averaged MEG spike started ~4 mm anterior to the tuber evolving in inferior direction. The ECD trace localized to the averaged EEG data started inferior to the tuber at the spike onset moving on the lateral posterior side to a localization ~5 mm superior to the tuber. MNEs confirmed the ECDs localizations at the peak of the two spikes.

Our results demonstrate that different generators may be responsible for the interictal spikes detected with MEG and EEG at the sensor level. Simultaneous MEG and EEG recordings are required in clinical practice to form a complete picture regarding the underlying epileptogenic generators.

P4-030

MEASUREMENTS OF COMPLEXITY AND OSCILLATIONS UNDER DIFFERENT COGNITIVE LOADS

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Introduction: Entropy commonly refers to a measure of "disorder" within a physical system. This metric can be used to analyse electrophysiological data where it is considered to measure complexity within neural networks. Rank Vector Entropy1 (RVE) measures the temporal evolution of complexity within a location of interest (LOI) in the brain. Here, we apply RVE to neuronal activity measured during two equivalent tasks with different cognitive load to test the hypothesis that entropy in the visual network is modulated by cognitive demand.

Methods: Ten participants completed two conditions of a Sternberg task: a cognitive load condition (CLC), where participants were required to encode and retain two visual stimuli, and a no load condition (NLC), where participants viewed the same paradigm but were instructed to passively respond regardless of content. A SAM beamformer (30-70Hz) identified LOIs in the visual and left motor regions for each task. Virtual electrode (VE) data from these LOIs were analysed using RVE. The entropy time courses were averaged across trials and participants. To further assess the visual response, a group level time-frequency analysis was also performed.

Results and discussion: Data from the visual LOI revealed that, during the encoding window, the CLC condition had significantly (p=0.01) lower entropy than the NCL condition. The time courses obtained from the motor cortex revealed no significant changes in entropy between tasks. The time-frequency analysis revealed a beta synchronisation (2.9 nAm +/- 0.3 nAm) within the encoding phase of the trial, which was significantly (p=.049) greater in the CLC than the NCL condition. The results suggest a close relationship between the metrics of power and RVE. However, the RVE is not solely dependent on power and in this scenario was more sensitive to neuronal differences between conditions.

1 Robinson SE, et al (2013) Front. Comput. Neurosci. 6:101.

P4-031

EXAMINING THE EFFECTS OF WITHIN-SESSION MOTOR LEARNING ON BRAIN ACTIVITY OBTAINED USING MEG

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Motor learning is described as performance improvement, or the ability to improve a new skill via repetitive practice and the provision of feedback. Despite a rapidly growing body of motor learning literature, regional changes in brain activity occurring during the initial stage of motor skill acquisition have not been adequately determined in humans. Previous studies using indirect measures of brain activity such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) suffer from methodological limitations, and have been largely focused on motor learning occurring between sessions of practice. The current study seeks to determine the brain areas underlying motor learning during a single session (approximately one hour) using magnetoencephalography (MEG). Healthy control participants (N=18; aged 25.2±4.5 years) performed a visuomotor task requiring a unilateral power grip to accurately move a cursor to a moving target. Learning was assessed by comparing behavioural measures (accuracy and error magnitude) pre- and post-training. Whole head dual-state beamformer analysis was applied to MEG data to identify regions of event-related synchronization/desynchronization (ERS/ERD) in the beta band (15-30 Hz). Respective changes in accuracy ($p < 0.05$) and error magnitude ($p < 0.05$) from pre- to post-training were associated with learning-dependent change in regions characteristic of motor networks. Analysis of whole-head beamformer localization showed learning-dependent changes in regions of interest ($p < 0.05$) including cortical and subcortical regions. Further analysis of these regions of interest from pre- to post-training was performed to investigate the timing of beta band ERS/ERD. The results of the current study add to the understanding of the neural structures involved in motor learning, highlighting the pre- to post-training changes in activation with high temporal resolution. Lastly, these results help in determining regions of interest for further elucidation using stimulation studies to establish the causal link between neuronal activity and learning phenomena.

P4-032

HYPERSCANNING MEG FOR UNDERSTANDING MOTHER–CHILD CEREBRAL INTERACTIONS

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Child development is strongly affected by social interactions with caregivers, which may lead to molding of later social behaviour in our daily life. However, the underlying neural mechanism for such interactions has not yet been revealed. We introduce a magnetoencephalographic (MEG) hyperscanning

system to examine brain-to-brain interactions between a mother and her child.

We used two whole-head MEG systems placed in the same magnetically-shielded room. One is a 160-channel gradiometer system for an adult and the other is a 151-channel gradiometer system for a child. We developed an audio-visual presentation system, which enabled a mother and her child to look at each other in real time. In each MEG system, a video camera was placed behind a half-mirror screen for visual presentation to obtain the subjects' facial expressions. The visual presentation system is capable of displaying not only real-time facial expression but also processed facial expression such as a still face or delayed facial expressions. A projector system displays the side-by-side face images of the mother and child, and the images are divided into each face using splitting mirrors and each face is displayed on the half-mirror screen in front of the other subject.

To the best of our knowledge, our system is the first MEG hyperscanning system in a single shielded room, and may contribute to elucidating brain-to-brain interactions not only between a mother and her child but also in general inter-individual, brain-to-brain interactions.

P4-033

THE ROLES OF NEURAL PHASE-RESETTING AND WHITE MATTER HEALTH IN INFORMATION PROCESSING SPEEDS OF HEALTHY CHILDREN AND CHILDREN TREATED FOR BRAIN TUMOURS

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Information processing speeds are consistently slower in children treated with cranial radiation (CRT) for brain tumours. Increased white matter damage following treatment predicts slower processing speeds in these children. Phase-Locking Factor (PLF) measures the phase-resetting capacity of a group of neurons to an event and is influenced by white matter structure. In healthy individuals, PLF increases in attentional regions to an attend-cue during the preparation phase of a task, and again to a response-cue during the execution phase of a task, and is associated with better task performance. We asked whether PLF during task preparation was related to performance and whether measures of white matter architecture predicted PLF and/or task performance in healthy children and children treated with CRT for brain tumours.

Results showed that multiple cortical regions were active in both healthy children and patients after presentation of a visual cue that alerted of an impending visual stimulus. Strongest activations occurred in the visual cortex (VI) and the posterior cingulate cortex (PCC) in both groups. Phase-locking was observed in the 13-29Hz (beta) spectrum in both of these regions and was significantly greater in healthy children than patients. Greater beta phase-locking values in VI and PCC predicted faster reaction times in the execution phase in all children. Fractional Anisotropy (FA: an index of white matter health) of whole-brain white matter was greater in healthy children and also predicted response times in healthy children, but not in patients. Moreover, greater FA also predicted greater PLF in healthy children, but not in patients.

We propose that white matter architecture influences information processing speeds, in part, through a phase-resetting within the beta band in both primary sensory regions (VI) and attention-related regions (PCC) and that white matter damage leads to a temporal inconsistency of the neural response which inhibits peak task performance.

P4-034

SIMULTANEOUS RECORDING OF MEG, EEG AND INTRACEREBRAL EEG DURING VISUAL STIMULATION: FROM FEASIBILITY TO SINGLE-TRIAL ANALYSIS

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Electroencephalography (EEG), magnetoencephalography (MEG), and intracerebral stereotaxic EEG (SEEG) are three neurophysiological recording techniques, which are thought to capture the same type of brain activity. Still, the relationships between non-invasive (EEG, MEG) and invasive (SEEG) signals remain to be further investigated. In early attempts at comparing SEEG with either EEG or MEG, the recordings were performed separately for each modality. However such an approach presents substantial limitations in terms of signal analysis. The goal of this technical note is to investigate the feasibility of simultaneously recording these three signal modalities (EEG, MEG and SEEG), and to provide a methodological framework to analyze this new kind of data. Intracerebral electrodes, for presurgical evaluation purposes, were implanted in a patient with intractable epilepsy. A visual stimulation paradigm was presented to the patient. Firstly, the analysis included a characterization of the MEG artifact caused by the SEEG equipment. Next, average evoked activities were computed at the sensor level, and cortical source activations were estimated for both the EEG and MEG recordings; these were shown to be compatible with the spatiotemporal dynamics of the SEEG signals. In the average time-frequency domain, concordant patterns between the MEG/EEG and SEEG recordings were found below the 40 Hz level. Finally, a fine-grained coupling between the amplitudes of the three recording modalities was detected in the time domain, at the level of single evoked responses. Importantly, these correlations have shown a high level of spatial and temporal specificity. These findings provide a case for the ability of trimodal recordings (EEG, MEG, and SEEG) to reach a greater level of specificity in the investigation of brain signals and functions.

P4-035
IMAGING AFFECTIVE PROSODY IN 5-DIMENSIONS

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Humans communicate emotion vocally by modulating acoustic cues such as pitch, intensity and voice quality (prosody). Previously using fMRI, we demonstrated how the relative presence or absence of such cues (cue-saliency) alters the likelihood of perceiving an emotion. These signal-driven perceptual changes were reflected in a reciprocal circuit consisting of superior and middle temporal gyrus (STG/MTG), amygdala and inferior frontal gyrus (IFG): Increased cue-saliency was associated with increased activation in STG/MTG and amygdala. Decreased saliency and hence higher ambiguity of emotional intention was associated with increased IFG activity and STG/MTG –IFG connectivity. Here, using this parametric approach with combined EEG-MEG recording, we explore the temporal-spectral dynamics of prosodic processing in fifteen healthy subjects.

Employing L2 Minimum-Norm Estimate (MNE) source modeling of our EEG-MEG data, we observed evoked activity changes that we divided into four temporal phases: Phase-1 activity (< 200ms Post-Stimulus Onset (PSO)) revealed right-lateralized STG/MTG activation. In Phase 2 (200-400ms PSO), activity shifted briefly to precuneus and then subsequently to orbitofrontal cortex (OFC). In Phase-3 (400 to 1000ms PSO), OFC sources continued to display activity with activation increasing first in right and then left IFG. During Phase 4 (1000-1900ms PSO), right IFG predominated with periodic coactivity in STG/MTG and sustained activity in medial aspects of OFC.

Modulation of emotional cue-saliency across stimuli indicated a complex temporal-spectral pattern: Increasing cue-salience correlated with increased right STG/MTG beta and gamma power within the Phase-1 window. Within right IFG, saliency correlated gamma and beta power increases were observed only midway through Phase-2. In contrast, cue salience decreases correlated with early Phase-1 beta and gamma power increases in right IFG and left MTG. In summary, the laterality and timing of activity within the temporo-frontal prosodic circuit is modulated in a frequency specific manner by the degree of signal ambiguity.

P4-036
INCREASED ALPHA AND CONCOMITANT FUNCTIONAL DECOUPLING OF IPL PREDISPOSES PERCEPTION OF AUDIOTACTILE SIMULTANEITY

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In this MEG study we aimed to investigate neural processes underlying the perception of integration or segregation of audiotactile signals in close temporal proximity. Participants were presented with a one-second sound of a mosquito approaching the head from the left side and with a spatially correlated tactile stimulus. By using different stimulus onset asynchronies (SOAs) between the offset of the sound and the touch, percepts were either "integrated" (i.e. it was the approaching mosquito that touched them) or "segregated" (i.e. the approaching mosquito was unrelated to the touch). By means of a staircase procedure, we first individually calculated at which SOAs the stimuli were ambiguous, i.e. response's rate integration/segregation was at 50%. In the subsequent MEG experiment, data were recorded with SOAs set to match this response's rate and perceptual reports were collected on a trial-by-trial basis. In this way, we could directly compare physically identical bimodal stimuli that elicited different (integrated or segregated) percepts. Perceptual audiotactile integration relative to segregation was characterized by following features:

3. in sensor space, an increase of power in the alpha band in a 350 ms time window preceding the tactile stimulus.
4. the generator of the alpha effect was located in a contralateral region centered at the caudal part of inferior parietal lobule (IPL).
5. For the time window of (1), phase synchrony revealed IPL to decouple from auditory and sensorimotor cortex and to synchronize with frontal areas

Integrated percept of ambiguously related multisensory auditotactile stimuli appears to be brain state dependent. Integration appears to be predisposed by decoupling of a multisensory region from more primary areas and by its coupling with prefrontal regions. These findings could possibly reflect interactions between bottom-up and top-down paths.

P4-037
THE SENSITIVITY OF MEG AND EEG TO CORTICAL ANATOMY

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While MEG and EEG can measure neuronal activity at the cortex, their sensitivity is closely related to the orientations of neuronal currents. The relative magnitude of MEG signal has been previously studied experimentally in animals and humans at a few locations. Recently, the sensitivity of MEG and EEG has also been calculated numerically based on realistic human brain models. However, the dependence of the sensitivity of MEG and EEG measurement on local cortical surface orientations and folding patterns remains unexplored.

Here we used high spatial resolution magnetic resonance imaging across 40 subjects to investigate the MEG and EEG sensitivity. Particularly, we calculated how normally oriented neuronal current sources contributed to MEG and EEG signals. Specifically, the forward solution of MEG and EEG at approximately 5,000 locations on the cortical surfaces was first calculated using Boundary Element Model. The sensitivity of MEG and EEG at each cortical location was then calculated by projecting the local forward solution

onto the direction perpendicular to the local cortical surface. We found that after considering the anatomy, MEG and EEG show clear and distinct sensitivity to neuronal currents at sulci and gyri across the whole brain. Such results can be useful in designing MEG and EEG experiments in terms of the number of trials and the expected signal-to-noise ratio if the activated neuronal areas are known a priori.

P4-038

RESTING STATE BRAIN CORTICAL ACTIVATION CHANGES IN PATIENTS WITH MIGRAINE: A MEG STUDY

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The cerebral cortex serves a primary role in the pathogenesis of migraine. This aberrant brain activation in migraine can be noninvasively detected with magnetoencephalography (MEG). The object of this study was to investigate the resting state cortical activation differences between migraineurs and controls and its related clinical characteristics by analyzing from low (1-4 Hz) to very high (1000-2000 Hz)-frequency ranges neuromagnetic signals. Twenty-two subjects with an acute migraine were compared to twenty-two age- and gender-matched controls using MEG. MEG scans were recorded 120 seconds during the headache attack. The signal was analyzed by the MEGProcessor in multi-frequency ranges. In comparison with the controls, migraine cerebral cortex activation area is different from controls in two frequency ranges (55-90 Hz, $p=0.001<0.05$) and (90-200 Hz, $p=0.004<0.05$). But the power value showed no significant differences between control and migraines in any frequency range ($p>0.05$). All the clinical characteristics had no significant correlation with aberrant brain activation. The results demonstrated that migraine subjects in resting state had significantly aberrant ictal brain activation in activation area that can be measured with neuromagnetic imaging techniques. The findings may facilitate the development of new therapeutic strategies in migraine treatment via alterations in cortical excitability with TMS and other medications in the future.

P4-039

INTEGRATION OF FMRI AND MEG FOR OPTIMIZED SPATIAL SENSITIVITY TO NEURAL ACTIVITY

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Functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) are two widely used neuroimaging techniques which operate on different mechanisms to measure brain activity, and possess unique spatial sensitivity profiles. Studies that examine activity in both deeper structures, to which MEG shows reduced sensitivity, and structures near air-tissue interfaces, in which fMRI signal can be distorted or lost, may benefit from integration of the two imaging techniques. The present study optimized sensitivity to neural activity by integrating fMRI and MEG data sets, using a novel method of weighting the inputs from the two modalities by a data-driven, voxel-by-voxel measure of quality. The method of integration was demonstrated using data from a visual object recognition task. MEG data were localized using beamforming to produce maps of activity comparable to fMRI activation maps. Data quality (contrast-to-noise ratio) was calculated at each voxel for each modality and was used to weight the contribution of that modality to the multimodal activation map. The resulting maps reflected both activations that were observed in one but not the other modality (e.g., hippocampus only in fMRI), and critically showed increased sensitivity to activation that was common to both modalities. This increased sensitivity resulted in detection of activations that were present, but below threshold, in both single-modality statistical maps. This demonstrates an improvement over both simple averaging of maps from two modalities, which leads to reduced sensitivity, and over fMRI-constrained MEG source localization, which negates any unique sensitivity of MEG.

P4-040

THE RELATIONSHIP BETWEEN NEUROTRANSMITTERS AND NEURAL OSCILLATION DURING WORKING MEMORY TASK: A COMBINED MAGNETIC RESONANCE SPECTROSCOPY AND MAGNETOENCEPHALOGRAPHY STUDY

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Introduction: To date, there are many findings of the relationship between neurotransmitters such as gamma-aminobutyric acid (GABA) or glutamate and neural oscillation in vitro studies closely related to psychiatric disorders such as schizophrenia. However, only a few studies have investigated the relation between these neurotransmitters and neural oscillation in the human brain. Here, we investigated the relationship between baseline GABA and (glutamate + glutamine) Glx concentrations at the resting state using magnetic resonance spectroscopy (MRS) and neural oscillation during a working memory task using magnetoencephalography (MEG) in the perigenual ACC (pgACC), the mid-ACC, and occipital cortex (OC).

Methods: We acquired MRS data at rest and MEG data during two-back task using 306ch whole head MEG (Neuromag) from 10 healthy male volunteers (mean age 24.9, SD 5.9). The GABA/Cr and Glx/Cr ratios were measured by AMARES package (jMRUI softwere), and corrected for the relative volume of the gray matter within each volume of interest (VOI). We analyzed the MEG data using MNE and FreeSurfer (Martinos Center for Biomedical Imaging), and evaluated the power spectral density (PSD) difference with the task load among two-back, one-back, and zero-back task

as two-backzero-back-zPSD (two-back value normalized by zero-back), two-backone-back-zPSD, and one-backzero-back-zPSD at theta (5-7Hz), alpha (8-12Hz), beta (15-29Hz), gamma1 (30-59Hz), and gamma2 (60-90Hz) frequency band during task (0 to 2 sec after visual stimuli) within each VOI. We calculated the Pearson correlation among the zPSD of each band, GABA/Cr and Glx/Cr within each VOI.

Results: The accuracy rate of two-back task was negatively correlated with theta and alpha band one-backzero-back-zPSD in the OC.

Conclusions: This result indicates that the degree of inhibition with task demand in the OC is correlated the efficient working memory processing.

P4-041

DIAGNOSTIC APPLICATION OF MAGNETOENCEPHALOGRAPHY FOR DETECTION OF EPILEPTOGENIC CORTICAL LESION IN MRI STUDY

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Rationale: We have tried to examine whether the initial negative radiological findings of focal cortical dysplasia (FCD) that is major cause of intractable epilepsy could be corrected by the MEG guidance.

Method: We have examined 51 cases with epilepsy whose initial MRI findings were normal, but MEG showed the positive findings of FCD. We provided the MRI of each subjects with MEG findings for the three board certified radiologists and asked whether they would like to change their initial negative impression about the existence of FCD.

Results: Two out of three radiologists changed their impression in 6 cases (11.7%). One out of three radiologists confirmed abnormal finding in 10 cases (19.6%). No case has been reconfirmed as FCD by all three radiologists. Twenty two cases (43.1%) have confirmed as initial diagnosis. Final diagnosis has been postponed in 13 cases (25.4%) by all three radiologists, since the findings were ambiguous or low resolution of the images at the area where MEG findings showed the existence of FCD.

Discussion: FCD was classified as Type Ia, Ib, IIa and IIb by Palimini in regards to existence of dysmorphic neurons. FCD Type IIb is supposed be a major cause of intractable epilepsy and regarded as one of the best candidates of epileptic surgery. FCD type IIb can be detected by MRI, since the density of dysmorphic neurons is high. In contrast, FCD type Ia, Ib and IIa has low density of dysmorphic neurons and MRI sometimes cannot show the lesion successfully. Our study shows the application of MEG guided MRI study for detection of FCD and efficacy of MEG for favorable outcome of epileptic surgery.

P4-042

EXPANDING THE LIMITS OF IMAGING TECHNOLOGIES: A COMBINED MEG AND FMRI INVESTIGATION OF HUMAN OBJECT REPRESENTATIONS

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A comprehensive understanding of the neural basis of brain function requires resolving both the spatial and temporal information of brain activity. The most common type of brain scan, fMRI, identifies the anatomical substrate of neuronal activation, but is too slow to capture millisecond brain dynamics. MEG measures neuronal activation with high temporal accuracy, but has a highly non-isotropic spatial resolution and does not reveal the precise location of these signals. Establishing correspondence across these imaging modalities remains a challenging problem, far more complex than simply achieving spatial correspondency mappings; different imaging techniques sample brain activity in fundamentally different ways and necessitate complex transformations from one modality to another. The principled limitations of combining MEG and fMRI modalities are well-established: electrophysiological and hemodynamic activity can be decoupled (BOLD and electrophysiological activity may not co-occur for physiological reasons), or suffer from signal detection failure (false positive/negative results in either modality). Here, we propose a novel way to combine imaging techniques that merges the time and location information of MEG and fMRI scanners using a computational approach called representational similarity analysis (RSA), which relies on the fact that two similar objects (such as two human faces) that produce similar signals in MEG will also produce similar signals in fMRI. We introduced the technique in our recent work (Cichy, Pantazis, Oliva Nature Neuroscience, 2014), proving that this approach is not only feasible, but promises a rich design for many novel findings. We recorded MEG and fMRI responses to 92 object images. We show that we can estimate the timing of object categorization in the first stages of human vision, and discriminate transient from persistent neural signals during visual object processing. We also illustrate how to extend the approach across species (macaque monkeys).

P4-043

PROCESSING PIPELINE FOR FUNCTIONAL LOCALIZATION WITH MULTIMODAL DATA

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Functional localization of motor tasks in both patients and healthy subjects is performed using multimodality imagery, namely fMRI (Siemens 1.5T), MEG (Elekta Neuromag) and high resolution EEG (128 sensors). The given functional mapping is expected to be used as a presurgical evaluation tool for ECoG implant positioning. The data are processed in a fully-integrated analysis pipeline using Brainstorm. Functional localization in MEG and EEG

is done by means of both weighted Minimum Norm Estimate (wMNE) and a Clinatec-made correlation-based method. fMRI localization is done with SPM 7.0.

The localization pipeline includes two manual steps which are performed at the very beginning:

a. Writing of a parameter file by means of a graphic user interface or a text editor. Such a file gives the ability to precisely fit the processing batch (e.g. epoch length, artifact discarding threshold, range of frequency analysis, etc.).
b. For accuracy purpose, registration of the fiducials on the MRI is operated manually in accordance with the neurosurgical team.

Then, for a given subject, the localization pipeline automatically detects and treats the different tasks of the acquired data. Traceability of the successive steps is ensured by log files which are automatically generated in the course of the process.

The final display enables to select and save regions of interest (ROIs) from a graphic user interface. The ROIs can later be superimposed across tasks, across modalities or across types of processing.These data are available for direct integration in MRI slices and transfer to a DICOM compliant surgical navigation device.

P4-044

EFFECT OF CONDUCTIVITY INHOMOGENEITIES ON MAGNETIC FIELDS DETECTED BY MEG AND NEURONAL CURRENT MRI

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Inhomogeneities in electrical conductivity may significantly distort the evoked magnetic field (MEF) due to primary neuronal currents. Prior theoretical analysis by Huang, Nicholson and Okada [1] showed that in the case of an isolated turtle cerebellum, the conductivity boundary between the cerebellar tissue (1.33 S/m) and the physiological saline (0.2 S/m) could significantly enhance the MEF by a factor of up to two. Using a BEM simulation of the same model, we will examine the effect of conductivity boundaries on the MEG signal 17mm away as well as on the neuronal current MRI (ncMRI) signal detected at the source location. We expect that the boundaries will increase the peak value and the spatial distribution of the detected field but leave the temporal waveform of the MEF unchanged. It is known that MEG measures the magnetic field produced by intracellular currents in active neurons a small distance from the source [2]. The ncMRI signal detects one component of the same magnetic field at the source location [3]. Understanding the effect of conductivity boundaries on these two signals could help improve detectability of neuronal magnetic fields with MRI.

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P4-045

THE RELATIONSHIP BETWEEN NEUROTRANSMITTERS AND NEURAL OSCILLATION DURING RESTING STATE: A COMBINED MAGNETIC RESONANCE SPECTROSCOPY AND MAGNETOENCEPHALOGRAPHY STUDY

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Introduction: To date, there are many findings of the relationship between neurotransmitters such as gamma-aminobutyric acid (GABA) or glutamate and neural oscillation in vitro studies closely related to psychiatric disorders such as schizophrenia. However, only a few studies have investigated the relation between these neurotransmitters and neural oscillation in the human brain. Here, we investigated the relationship between baseline GABA and glutamate + glutamine (Glx) concentrations using magnetic resonance spectroscopy (MRS) and neural oscillation at the resting state using magnetoencephalography (MEG) in the perigenual ACC (pgACC), the mid-ACC, and occipital cortex (OC).

Methods: We acquired MRS and MEG data at the resting state using 306ch whole head MEG (Neuromag) from 12 healthy male volunteers (mean age 26.7, SD 6.5). The GABA/Cr and Glx/Cr ratios were measured by AMARES package (jMRUI software), and corrected for the relative volume of the gray matter within each volume of interest (VOI). We recorded the resting MEG data for 420 seconds with the eyes closed at the upright position. We analyzed the MEG data using FreeSurfer (Martinos Center for Biomedical Imaging) and Brainstorm (Tadel et al. 2011), and evaluated the power spectral density (PSD) difference at theta (5-7Hz), alpha (8-12Hz), beta (15-29Hz), gamma1 (30-59Hz), and gamma2 (60-90Hz) frequency band within each VOI. We investigated the difference of the GABA/Cr and the Glx/Cr, and the PSD of each frequency band among these VOIs using two-way ANOVA.

Results: The GABA/Cr in the pgACC was lower than those in the mid-ACC and OC, and the Glx/Cr in the mid-ACC was higher than those in the pgACC and OC. There was no difference of the PSD among these VOIs.

Conclusion: These results indicate that the different concentrations of GABA and Glx between pgACC, mid-ACC, and OC, and that the comparable level of PSDs regardless of frequency band.

P4-046

EVENT-RELATED THETA POWER IS ATTENUATED BY ALCOHOL INTOXICATION AS A FUNCTION OF RESPONSE CONFLICT DIFFICULTY

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Alcohol intoxication is known to impair decision making, but performance is not compromised to an equal degree in all circumstances. The present study investigated the effects of moderate alcohol intoxication on event-related theta band (4-7Hz) oscillations during response conflict elicited by two variants of the Simon task differing in difficulty. In the Simon-Choice (SC) task, red or green squares were presented on the left and right side of the screen. Simon-Stroop (SS) was a more difficult, hybrid task in which the words 'left' and 'right' were presented centrally in red or green letters. In both cases, subjects were asked to respond only to the color of the stimulus. Healthy social drinkers participated in both alcohol (0.6 g/kg ethanol for men, 0.55 g/kg for women) and placebo conditions in a counterbalanced design. Whole head MEG and select scalp EEG signals were acquired. Each trial was decomposed using Morlet wavelets and theta power estimates were obtained using an anatomically-constrained, noise-normalized, distributed minimum norm inverse model. Subjects responded more slowly and less accurately to incongruous stimuli in the SS as compared to the SC task. Response conflict increased event-related theta power during both tasks in a bilateral network including the medial and ventrolateral prefrontal cortices. Theta power during SC conflict was observed as a unitary peak, centered at ~325ms post-stimulus in the anterior medial prefrontal cortex, while during SL conflict, a later and sustained increase centered in the anterior cingulate cortex was seen. In SC, event-related theta power was attenuated by alcohol intoxication overall, but in the more cognitively demanding SS task, intoxication selectively reduced theta power only during incongruous trials. These finding are consistent with previous studies suggesting that alcohol impairment disproportionally affects high-level, complex cognitive control functions.

P4-047

OSCILLATORY ALTERATIONS OF RESTING-STATE BRAIN NETWORKS IN CHILDREN BORN VERY PRETERM

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Although resting-state networks (RSNs) have been traditionally investigated using functional magnetic resonance imaging (fMRI), recent advances have shown RSN's can also be imaged using magnetoencephalography (MEG). Moreover, MEG allows direct measurement of neurophysiological oscillations with high temporal resolution. Children born very prematurely (≤32 weeks) frequently experience selective cognitive difficulties, even in the absence of major neurological or intellectual impairment. The biological underpinnings of such problems remain poorly understood, but mounting evidence has implicated the atypical development of structural and functional networks. In the present study, two minutes of resting-state MEG activity was recorded from 26 very preterm children and 26 matched controls (mean age=7.7 years). The data were filtered into physiologically relevant frequency ranges: theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-50 Hz). Source activity was reconstructed using a linearly constrained minimum variance beamformer throughout brain space. Independent Component Analysis (ICA) was applied to the Hilbert envelope of the temporally smoothed source activity resulting in spatio-temporal RSNs. Resting-state networks including the auditory, cerebellum and potentially an immature default mode network (DMN) were observed primarily in the theta-, alpha- and beta-bands in both groups with similar spatial patterns. However, the RSNs in the preterm children were observed in slower frequency ranges. For example, the DMN was observed in the alpha-band for the preterm group compared to the beta-band for the control group. These results indicate that intrinsic connectivity among functionally related brain areas is organized at a slower frequency in children born very preterm. In light of prior research linking atypical resting-state MEG oscillations to increased neonatal pain-related stress and poorer cognitive outcome, these findings suggest that adverse neonatal experience may interfere with the development of neurophysiological interactions within functional networks, resulting in problems with cognitive development in these vulnerable children.

P4-048

CHARACTERIZATION OF PATHOLOGICAL PERILESIONAL ACTIVITY IN STROKE USING MULTISCALE ENTROPY

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In brain disorders that involve frank structural lesions, such as tumour and stroke, there is a preponderance of pathological low frequency activity originating from perilesional sources. Recently, there has been emerging interest in the use of multiscale entropy (MSE) to further characterize pathological neural activity. MSE belongs in a family of nonlinear measures which assess signal complexity: the degree to which a signal is not completely random, but also not completely periodic. Importantly, spontaneous signals measured from dynamical biological systems like a healthy brain are high in complexity. Furthermore, disorders that cause structural lesions have been associated with a reduction in signal complexity. Unfortunately, nonlinear measures are not compatible with traditional source localization techniques

like LORETA and delta dipole localization. Thus, while pathological low frequency activity has been successfully localized to perilesional regions, perilesional signal complexity has yet to be assessed. Using beamformer-based source localization of resting state MEG signals, we assessed signal complexity and spectral power in stroke patients with left hemisphere lesions, who were compared against age-matched and young controls. Both MSE and spectral power were sensitive to dysfunctional perilesional tissue, though the reduction in MSE was observed along a greater spatial extent. Furthermore, aging was also associated with changes in spectral power but not MSE. Decreased MSE was associated with a lack of functional activation on a language task, and with hypoperfusion as assessed with arterial spin labeling. The present results suggest that nonlinear measures like MSE are more sensitive to dysfunctional perilesional tissue, when compared to spectral-based measures, which is also sensitive to aging.

P4-049

PRIMARY MOTOR CORTEX MAPPING IN BRAIN-LESIONED PATIENTS USING MEG RESTING-STATE

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Introduction: The use of resting-state activity for preoperative functional mapping represents a potential alternative to task-related localization in brain-lesioned patients. It requires minimal patient collaboration, avoids task-performance confounds and allows investigating several brain systems. This study tested the ability of MEG resting-state functional connectivity (rsFC) analysis to map the primary motor hand area (M1ha) in a group of presurgical patients. This method is based on the strong resting-state connectivity between the left and right M1ha.

Methods: MEG resting-state data were recorded with a whole-scalp MEG (Elekta) in 10 presurgical patients (5 females, mean age: 37.7 years) with focal (6 patients) or hemispheric (3 patients) brain lesions, or refractory neuropathic pain (1 patient) (duration: 373±147s (mean±std), eyes open: 7 patients, eyes closed: 3 patients). MEG data (bandpass: 0.1-45Hz) were corrected for eye-movement and cardiac artifacts using independent component analysis. Source reconstruction was performed using a spherical conductor model determined from patient's MRI and β-band (12-21Hz) Minimum Norm Estimation. M1ha seed-based rsFC maps were obtained using slow source Hilbert envelope correlation from a seed located in the non-affected M1ha (MNI coordinates based on functional mapping literature). The localization of the correlation maximum in the hemisphere contralateral to the seed was compared to classical MEG or fMRI functional indicator(s).

Results: In all patients, rsFC maps displayed inter-hemispheric resting-state connectivity. In 7 patients, a good concordance between the correlation maximum located in the hemisphere contralateral to the seed and functional indicator(s) was found. In 1 patient, one local correlation maximum colocalized with functional indicators.

Conclusion: This study suggests that MEG resting-state is able to map the M1ha in presurgical patients with brain disorders. Therefore, MEG resting-state might represent an interesting alternative to task-related functional mapping that should be considered as an additional functional indicator in the armamentarium of MEG M1ha mapping methods.

P4-050

UBIQUITOUS LOW-FREQUENCY PHASE DURING REST AND VISUAL STIMULATION COUPLES TO EVOKED GAMMA RESPONSE

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Cross-frequency coupling between the phase of low-frequency neural oscillations and their amplitude (PAC) in the gamma range has been attributed a key role in the processing of information (Canolty and Knight 2010). To test whether PAC within one area is unaltered over several rest sessions and when a task is performed, we used visual stimulation, which evokes a strong subject specific gamma response (van Pelt et al., 2012).

14 healthy subjects were recorded in a 275 channel CTF system (21 - 45 years; 5 female). The MEG recording started with 5 minutes of rest in a seated position with eyes-open. Afterwards subjects were presented with visual stimulation consisting of inwards moving circles (Hoogenboom et al., 2006). After visual stimulation subjects had a 15 minute break and then a final 5 minutes of rest were recorded.

For MEG recordings a forward solution and the constrained minimum norm imaging kernel were computed with Brainstorm (Tadel et al., 2011). We employed a Morlet-based time-frequency decomposition to extract the main evoked gamma response from the visual stimulation. Then the phase-amplitude coupling (PAC) (Ötzkurt and Schnitzler 2011) was calculated for the sources within V1 and V2 for the visual stimulation and the different rest periods.

We found no significant difference in PAC value between the resting periods before the visual stimulation and after the visual stimulation. This indicates that PAC is a consistent mechanism during rest. However, once the visual stimulation starts, the PAC value significantly increases.

For all visual areas the evoked gamma response was lower than the gamma frequency related to the maximal PAC. Yet, the low-frequency from the highest PAC during rest and the low-frequency coupling to the evoked visual gamma response stayed the same. Thus, the low-frequency phase is a constant pacemaker for the gamma oscillations during both rest and task.

P4-051
EEG CORRELATES OF COGNITION DURING THE RESTING STATE

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The human brain generates complex patterns of activity and cognition during wakeful rest, yet their relationship remains elusive. Despite great advances in characterizing resting-state neurophysiology, linking (electro)physiology to the rich inner experiences during the resting-state has received scant attention. To assess such experiences, we developed the Amsterdam Resting-State Questionnaire (ARSQ) of 54 items for rating feelings and thoughts experienced during wakeful rest. Using factor analysis, the ARSQ can be reduced to ten factors of resting-state cognition (Discontinuity of Mind, Theory of Mind, Self, Planning, Sleepiness, Comfort, and Somatic Awareness, Health Concern, Visual Thought, Verbal Thought). Here, we investigate relationships between cognition and brain activity during the resting state using the ARSQ and electroencephalography (EEG).

We recorded >111 subjects using 128-channel EEG during a five minutes eyes-closed rest session. The ARSQ was used to explore cognitive content of the participants directly after the session. EEG data were analyzed using the Neurophysiological Biomarker Toolbox (NBT, http://www.nbtwiki.net/), which is dedicated to the computation of a wide range of classical and novel biomarkers, and correlated these with the average factor sum scores derived from the ARSQ data.

We found significant ($p<.05$) negative correlations between alpha power [8-13 Hz] in fronto-parietal regions and the factor “Self” as well as significant positive correlations between normalized central delta-amplitude [1-4 Hz] and the factor “Sleepiness”.

Our results show that the ARSQ could prove useful for shedding light on functional implications of genetic or disease related variation by successfully combining electrophysiological and cognitive measures. Future analyses with novel EEG-biomarkers and measures of functional connectivity may reveal an even more detailed view on the link between electrophysiology and cognition.

P4-052
TRANSIENT SUPPRESSION OF GAMMA POWER IN THE DEFAULT-MODE AND VENTRAL ATTENTION NETWORK IN AN EMOTION DETECTION TASK

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Performing a high attention demanding task not only activates a fronto-parietal network, but also reduces the activity in the default mode network (DMN). Hemodynamics-based neuroimaging studies have largely reported DMN deactivation, however its functional significance remains debated and is difficult to resolve without access to its electrophysiological correlates and fine-scale temporal dynamics.We obtained intracranial EEG recordings from 11 epilepsy patients while they performed a facial expression detection task. We observed a strong task-related high gamma (60-140 Hz) power suppression following face presentation within the DMN and the ventral attentional network (VAN). The deactivation in these two networks was significantly weaker when a scramble image was presented, indicating that this transient response was specific to face processing and not systematic to visual stimuli. While the gamma-band deactivation (GBD) in the VAN and the DMN between the target emotion (fear) and the other face stimuli showed no difference in onset nor amplitude of the deactivation, we found that the duration of the GBD was significantly longer for the target stimuli. Interestingly, the length of the GBD differed among the various facial expressions used: The shortest GBD was observed for happy faces, followed successively by neutral, and disgusted faces and was longest for the fearful faces. Finally, to ensure that the GBD was not due to an automatic attentional capture by face stimuli, we presented the same face stimuli while the patients engaged in a low-attention demanding pop-out task. In this context, face presentations did not elicit GBD.

Our results provide novel insights into the electrophysiology of DMN deactivation and fine-tune our understanding of its functional role in terms of global attention engagement and detection of task-relevant stimuli. It also indicates that DMN deactivation durations can be modulated by the emotional similarity of the stimuli with respect to target emotion.

P4-053
THE ELECTRORETINOGRAM EXHIBITS EYES-CLOSED ALPHA OSCILLATIONS THAT COUPLE WITH VISUAL CORTEX

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Previous research in animals and our present research in humans have shown that high-frequency oscillatory responses can become synchronized between the retina and visual cortex, indicating that the retina may drive a component of high-frequency activity in cortical visual areas.

However, could ongoing cortical or thalamic oscillations possibly influence the retina? The presence of efferent connections from the brain to the retina is well-established in some animals, but remains controversial in primates, including humans. We hypothesized that, if such efferent connections exist in humans, then eyes-closed alpha waves may be transmissible to the retina.

We therefore simultaneously recorded MEG and electroretinography (ERG) with a DTL fiber electrode placed on the right eye of healthy human subjects, while they opened and closed their eyes in 30-second intervals.

In 8 of 9 subjects, we observed a substantial increase in alpha power in the ERG with eyes closed that corresponded (in 6 of these 8 subjects) with

power changes in the MEG signal. Indeed, alpha oscillations were often strikingly visible in the raw ERG traces. Preliminary analyses with retinocortical coherence (based on beamforming) suggest an increase in alpha-band connectivity between the ERG electrode and contralateral occipital areas for eyes closed blocks relative to eyes open. If confirmed, this would reduce the likelihood that the ERG alpha may be an artifact of rhythmic eye movements.

These findings point to a functional connection between retinal and cortical alpha activity, and may constitute evidence in support of efferent connections to the retina.

P4-054

EFFECT OF BDNF VAL66MET POLYMORPHISM ON LOW-ALPHA/GAMMA COUPLING OF SPONTANEOUS OSCILLATIONS IN PRIMARY DYSMENORRHEA

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Our previous studies based on multimodal neuroimaging techniques demonstrated that ongoing menstrual pain in primary dysmenorrhea (PDM) was accompanied by functional and structural changes in the brain. However, few studies examined effect of such cycling cramping pain on spontaneous oscillations in electrophysiological signals. Brain-derived neurotropic factor (BDNF) has been proposed to associate with cognitive and memory functions in several neurological and psychiatric disorders. We used cross-frequency phase-phase coupling as an indicator of functional connectivity to investigate whether BDNF Val66Met polymorphism contributes to the alteration of resting network in PDM. Fifty PDM and 49 healthy female controls were enrolled, including 30 Val/Val, 39 Val/Met, and 30 Met/Met. Resting magnetoencephalographic signals with 3-5 minutes of eye-open were recorded during the 1st-3rd day of the menstrual cycle (MENS) and the 12th-16th day of the menstrual cycle (POV). Morlet wavelet was adopted to estimate the cross-frequency phase-phase coupling. Separate two-way ANOVA (group x gene) test for each channel was conducted to examine the association between pain experience and BDNF Val66Met polymorphism in resting cross-frequency coupling. A significant interaction between gene and group of low-alpha/gamma coupling was found ($F=3.102$, $p=0.05$) in MENS phase. Further analysis showed decreased coupling of PDM Met/Met homozygotes than that of PDM Val carriers in the left central/temporal region. However, a significant gene-by-group interaction of low-beta/gamma coupling was found ($F=3.965$, $p=0.022$) in POV phase. The PDM Val/Val homozygotes had decreased coupling at the left temporal region than PDM with Met carriers had. Our results demonstrated the effect of the BDNF Val66Met polymorphism on the resting low-frequency/gamma coupling, which implicated that the BDNF homozygotes, either Val/Val or Met/Met, may modulate neural processes associated with body integration and pain perception. These findings suggest that examining genetic factors in close relation to neurophysiological processes appears as a promising approach in neuroscientific PDM research.

P4-055

SOURCES ANALYSIS OF RESTING STATE FUNCTIONAL CONNECTIVITY IN HEALTHY AGING AND MILD COGNITIVE IMPAIRMENT: INFLUENCE OF APOLIPOPROTEIN E POLYMORPHISM

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The Apolipoprotein E (APOE) ε4 allele is the major genetic risk factor for the development of late-onset Alzheimer's disease (AD) but how this genetic biomarker interacts with the neurodegeneration that occurs in early AD is unresolved. This study aimed to characterize the brain's functional organization in healthy and pathological aging by means of analyzing functional connectivity (FC) patterns in MEG resting state recordings in source space. To this end, subjects were classified according to their diagnosis (Controls vs MCI) and the APOE genotype (ε4 allele carriers vs non-carriers). FC differences were assessed through a two way ANOVA. When the diagnosis effect was studied, MCI patients exhibited a significant diminished FC in high frequency bands affecting medial temporal and parietal regions. This result correlated with cognitive decline and neuropsychological performance. Regarding the results of the APOE genotype effect, the ε4 allele carriers showed a decreased FC in the delta band between occipito-frontal regions. Finally, when the interactions between diagnosis and APOE genotype were analysed, we found that the FC pattern of the right fronto-temporal region could be reflecting a compensatory/disruption process within the ε4 allele carriers. Our investigation demonstrates that APOEε4 and diagnosis affect resting-state FC in different ways. Therefore, a combination of genetic and neurophysiological information might help to detect MCI patients at higher risk of conversion to AD, and asymptomatic subjects at higher risk of developing a manifest cognitive deterioration.

P4-056

THE SPATIOTEMPORAL OSCILLATORY EFFECTS OF SUBANAESTHETIC KETAMINE INFUSION IN MAN: A PHARMACO-MEG STUDY

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There has been a recent resurgence in interest in the NMDA receptor antagonist ketamine, following discovery of its rapid antidepressant properties. While detailed animal models of the molecular mechanisms underlying ketamine's effects have emerged, there are few MEG/EEG studies examining the acute subanaesthetic effects of ketamine infusion in man. We recorded 275 channel MEG in two experiments. In experiment one (n=19), we recorded a five minute resting baseline period and participants then received a bolus of 0.25 mg/kg ketamine followed by maintenance infusion (6.25 ug/kg/min). A further ten minutes of resting data were recorded followed by a set of basic tasks. In experiment two, the same infusion protocol was used, with the infusion lasting twenty minutes. No tasks were performed in experiment two (n=5) and eighty minutes of resting MEG data were recorded in order to track the temporal profile of ketamine effects. As expected, subanaesthetic ketamine doses caused increases in heart rate, blood pressure and decreases in saccadic eye movement velocity accompanied by strong subjective effects. MEG power spectra revealed a rich set of significant oscillatory changes compared to placebo sessions. This included a) decreases in delta power (1-4 Hz) in parietal, occipital and temporal cortices b) increases in medial frontal theta power (4-8 Hz) but occipital decreases c) decreases in occipital, parietal and anterior cingulate alpha power (8-13 Hz) d) decreases in occipital and temporal beta power (13-30 Hz) e) increases in frontal and temporal low gamma power (30-50 Hz) and f) increases in parietal and cingulate cortex high gamma power (50-100 Hz). In Experiment 2, spatiotemporal pharmacodynamic effects were mapped and the various changes in resting-state functional connectivity profiled. The rich set of effects observed could potentially serve as biomarkers of the rapid antidepressant effects of ketamine and future similar studies in clinical patients are warranted.

P4-057

ABNORMALITIES IN RESTING STATE CONNECTIVITY IN BIPOLAR DISORDER

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Bipolar disorder(BD) is characterized by episodes of depression, alternating with hypomania or mania. Recently, there has been increased interest in resting state imaging, particularly in mood disorders where ongoing cognitive processes may be particularly relevant. Functional MRI studies have indicated alterations in connectivity, particularly involving cortico-limbic circuitry1, although the electrophysiological correlates are unknown.

Seventeen depressed subjects with BD(12 medicated with lithium or valproate) and 16 healthy controls underwent 250s MEG recordings on a 275-channel CTF system. Recordings were filtered for the beta band(14-30Hz) and projected into anatomical space using synthetic aperture magnetometry(SAM)5. The Hilbert envelope was calculated, smoothed, and downsampled(1Hz). Images were Talairach aligned and mean corrected. Data from all subjects were concatenated and 25 independent components(ICs) were extracted using temporal ICA. Linear regression was used to obtain spatial maps for each IC for the combined group and each subject separately. ICs were compared between groups using t-tests. An initial voxel-wise threshold of $p<0.005$ was used, and lowered if necessary to distinguish individual clusters. Voxel-wise false discovery rate(FDR) and cluster-wise family-wise error(FWE) corrected p-values are reported.

Of the 25 IC's, 20 were distributed networks, familiar from the fMRI literature, or single nodes. BD subjects showed reduced bilateral connectivity within motor networks, as well as reduced connectivity between motor networks and amygdala, orbital cortex, and insula. BD subjects also showed reduced connectivity between a distributed network involving parahippocampal cortex, amygdala, and orbital cortices, with bilateral middle occipital cortex.

Our study implicates aberrant bilateral connectivity, and reduced connectivity between the amygdala and cortical regions, extending fMRI findings, and identifying beta band connectivity with the motor system as an area of particular importance. Further research into the electrophysiological underpinnings of abnormal connectivity may further elucidate the pathophysiology of BD.

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P4-058

RECONSTRUCTING RAPID DYNAMICS IN ENDOGENOUS BRAIN NETWORKS REVEALS FREQUENCY-SPECIFIC DIRECTIONAL INTERACTIONS

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There is an increasing amount of evidence that the brain does not behave as a passive stimulus-response system. Instead it is now considered that perception and cognition are active, ongoing processes which are modulated rather than initiated by stimuli and task demands. As such, even when a participant has no particular task to perform, low frequency modulations of BOLD activity with a robust spatio-temporal organisation have been observed and there is a growing literature on these endogenous or 'resting state' networks. Evidence from the computational literature suggests that the structure of these endogenous networks can arise from time-delayed interactions between coupled brain regions oscillating at much higher frequencies.

The present study seeks to characterise directed causal structure within these networks by modelling delayed interactions between observations at

nodes within the Default Mode Network (DMN) as measured using MEG in human subjects.

The rapid dynamics of the underlying system are first reconstructed using Time Delay Embedding (TDE) which naturally leads to the estimation of predictive causality measures using subset multivariate autoregressive (MVAR) models. The model parameters quantify the predictive power of each point in the TDE on the subsequent observations. The directionality of information flow within the DMN is then characterised in the frequency domain by estimating the Partial Directed Coherence from the fitted MVAR parameters.

As an optimal reconstruction of the underlying dynamics relies on an appropriate choice of both delay and model order, we perform a systematic search of this parameter space to identify a physiologically plausible region within which models are both stable and provide fine grained spectral resolution.

Through examinination of the medial prefrontal and posterior cingulate cortex—areas considered the 'hubs' of the DMN—we demonstrate frequency dependent connectivity profiles in which low and high frequencies are characterised by differing, and often reciprocal, directionality.

P4-059

REPEATABILITY OF OSCILLATORY RESTING STATE NETWORKS IN HEALTHY INDIVIDUALS

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The study of functional neural networks and how they map on to cognitive and sensory performance is a well established topic of neuroimaging research. Increasingly, there is a focus on understanding how these networks may be used to measure differences in functionality between groups, and whether these provide novel biomarkers of neurological or neuropsychiatric conditions. Most commonly this has been done using fMRI but recently developed techniques have enabled network analysis to be conducted on MEG data, which crucially do not rely on indirect measures of blood flow that may be compromised in clinical populations. For a biomarker to be meaningful it should be characteristically stable for an individual in the absence of disease or disorder, and only a handful of fMRI studies have investigated the intra-individual stability of these resting state networks (RSNs) over time. To our knowledge, no studies have examined the repeatability of MEG RSNs. Here, we investigated the test-test repeatability of RSNs that were derived from resting-state MEG data using an independent component analysis (ICA) approach [1]. Twenty-one healthy subjects underwent two resting-state recordings, one week apart. Following group ICA we examined two of the most robust components, representing the sensorimotor and visual networks in the beta band (13-30Hz). Activity within the network was indexed using a bootstrapped standard deviation of power within the component, and both networks showed inter-individual differences in this measure. Furthermore, intra-class correlation coefficients demonstrated high intra-individual repeatability across sessions. These results indicate that RSNs measured using MEG represent stable trait markers for individuals over time, and validates their use as a method of comparison in clinical populations.

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P4-060

A REAL-TIME IMAGING NEUROFEEDBACK IN MEG

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There is a considerable and renewed interest in brain-computer interface and a range of new therapeutic applications using biofeedback techniques, whereby subjects are informed in real-time of their performance in meeting a specified target based on physiological metrics. A major impediment to biofeedback so far, has been the limited specificity of measured signals. For instance, heart rate is only an indirect measure of stress levels; the smeared brain signals captured with a few electroencephalography (EEG) electrodes are nonspecific of targeted brain regions.

In the Neurospeed lab, we developed an approach to biofeedback, based on a real-time brain imaging with magnetoencephalography (MEG) system, having a unique combination of spatial specificity (to monitor activity emerging from predetermined brain regions) and temporal resolution (to monitor rapid processes in ongoing neural activities). In this real-time technique, all the processing steps from noise removal, to source imaging, and biometric extraction, are being performed online within only 22.5±1.1 ms. The other interesting fact is that the total delay of data acquisition, data transfer, and delivery of the feedback to the subject in the MEG room, is not more than 150 ms.

We also showed that targeting of pre-selected brain regions and training of specific components of time-resolved brain activities within these regions is possible with real-time MEG-imaging neurofeedback. To achieve this aim, two healthy volunteers were successfully trained to modify the neural oscillatory activities in a pre-defined region of their brain. This study opens new perspectives to the specific reinforcement of features of ongoing brain dynamics in targeted brain regions, with multiple potential cognitive and clinical applications.

In the next step, we employed this technique for training healthy volunteers, with low performance in near-threshold (6.25 cents) pitch discrimination, to see the effect of the training on their behavioral performance in this particular task.

P4-061

MEG-DTI IMAGING OF CONNECTIVITY IN CHILDREN BORN VERY PRETERM: CONVERGING STRUCTURAL AND FUNCTIONAL NETWORK ALTERATIONS

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Children born very preterm often exhibit learning and behavioural problems at school age, even among those free of apparent neurological impairment or with normal IQ. Magnetic resonance imaging (MRI) studies reveal smaller regional volumes and disruptions to white matter (WM) connectivity in children born very preterm. Whether resting-state MEG synchrony is altered in this population and how alterations in structural brain connectivity may influence neurophysiological network interactions is unknown. Combining diffusion tensor imaging (DTI) measures of WM connectivity with source-resolved MEG analysis provides a unique approach to link structural deficits with functional outcome. In this study, we collected spontaneous MEG data (151-channel CTF system) and 60-direction DTI data (Siemens 3T Trio MRI) in a cohort of 16 very preterm-born children and 16 full-term, age- and sex-matched control children. Beamformer analysis was used to reconstruct brain activity from all 116 cortical, subcortical and cerebellar regions in the AAL atlas. Neural synchrony (an estimate of functional connectivity) was measured using the weighted phase lag index in the theta, alpha, beta and gamma frequency ranges. After preprocessing the DTI data, BEDPOSTX and PROBTRACKX were used to calculate WM connectivity matrices between the same 116 regions.

We identified widespread, decreased functional connectivity in frontal, temporal, subcortical and cerebellar regions in all analyzed frequency ranges in the very preterm group. Further, decreased WM connectivity was associated with decreased functional synchrony in all bandwidths. Significant correlations between frontal, temporal and cerebellar WM connectivity and neural synchrony suggest behavioural implications for the structure/function relations subsequent to very preterm birth. This study provides the first source-resolved evidence of atypical resting state synchrony among brain regions in very preterm-born children, and uniquely demonstrates that these atypical neurophysiological network interactions are associated with alterations in structural networks.

P4-062

NETWORK DYNAMICS UNDERLYING VISUOSPATIAL ATTENTION CONTROL

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Selective visuospatial attention control has been shown to require a distributed network which encompasses occipital, parietal and frontal brain regions. The dynamics of activation and communication within this large-scale network remain poorly understood. In the present study, MEG was recorded while subjects performed in a Posner cueing paradigm, which required covert orienting of attention to either the left or right side of the visual field following a centrally presented directional cue. Inspection of time series of neuromagnetic activity in the cue-target interval revealed peaks of activity centred at 150ms, 230ms, 400ms and 930ms following stimulus onset, indicating a protracted sequence of brain activation during attention control. Event-related beamformer (ERB) analysis was used to localize activation during each peak in the MEG time series. This revealed sequential activation of task-relevant brain regions which began in occipital regions and later encompassed parietal, temporal and frontal areas. Significant activations were observed in left and right cuneus, right precuneus, intraparietal lobule, insula and anterior cingulate, left superior temporal gyrus, left and right inferior frontal gyrus, and left and right middle frontal gyrus. Beamformer reconstruction of broadband activity (1 – 150 Hz) from each significant regional activation was then performed, and transfer entropy was used as a directed index of inter-regional communication. This analysis revealed dynamic network communication supporting task performance. These results indicate the sequential activation and communication in a distributed network of brain regions underlies the control of visuospatial attention control, capitalizing on the combined spatial and temporal resolution of MEG to provide new insights into neural dynamics in attention orienting.

P4-063

FAST TRANSIENT NETWORKS IN SPONTANEOUS BRAIN ACTIVITY

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It has recently been shown that functional connectivity within large-scale networks of spontaneous activity exhibits temporal variability on a time scale of seconds to tens of seconds. However, in order to provide an effective substrate for cognitive processes, functional brain networks should be able to reorganise and coordinate on a sub-second temporal scale. We present a novel approach that identifies transient networks of brain activity, with no prior assumptions on the brain areas or time scales involved. The method is underpinned by a hidden Markov model (HMM), which infers a number of discrete brain states that recur at different points in time. Each inferred state corresponds to a unique pattern of whole-brain spontaneous activity, which is modelled by a multivariate normal distribution and a state time course indicating the points in time at which that state is active. These two outputs allow us to describe both the spatial and temporal characteristics of each inferred state. By applying this method to source projected MEG recordings of resting state activity, we identified transient (100-200 ms) brain states with spatial topographies similar to those of well-known resting

state networks (RSNs). By assessing temporal changes in the occurrence of these states, we demonstrate that within-network functional connectivity is underpinned by coordinated neuronal dynamics that fluctuate much more rapidly than has previously been shown. We further assessed cross-network interactions by studying the relationship between the inferred states and show that anticorrelation between the default mode and dorsal attention networks is consistent with an inability of the brain to transition directly between these transient states.

P4-064

RETINAL HIGH-FREQUENCY OSCILLATIONS DRIVE CORRESPONDING RHYTHMS IN CONTRALATERAL VISUAL CORTEX

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The retina is known to substantially preprocess visual stimuli, and some consider it to be an extension of the brain due to the sophistication of its neural circuitry. The electrical activity of the retina, or the electroretinogram (ERG), can be measured using special electrodes placed on or near the eye. While the ERG is widely used as a clinical diagnostic technique in ophthalmology, it is less known in human neuroscience research. Studies examining information transfer between retina and cerebral cortex in humans remain especially rare.

Visual stimuli have been shown to induce occipital gamma band activity in visual cortex that is measurable with MEG/EEG, and they have been suggested to reflect local information processing. However, visual stimuli also evoke retinal “oscillatory potentials” in similar frequency bands. We therefore hypothesized that a substantial portion of the visual cortical gamma band response may follow directly from retinal responses.

ERG was recorded simultaneously with whole-head MEG during flash stimulation. Visual cortex responses typically mirrored those of the retina with a delay of ~25 ms. The profile of high gamma band activity was similar between the two recordings, centered at approximately 100 Hz, with a phase delay of ~14 ms between visual cortex and the retina. Granger causality additionally suggested that a small amount of information also flows from cortex back to the retina.

Our results suggest that visually induced gamma band activity may in fact arise as a consequence of retinal processing, either in addition to or perhaps instead of local processing within visual cortex. Furthermore, in addition to communicating sensory information to the brain, the retina may receive measurable feedback or modulation from visual cortex.

P4-065

DO MICRO-SACCADIC EYE MOVEMENTS MODULATE VISUALLY INDUCED GAMMA OSCILLATIONS? AN MEG STUDY USING HIGH-SPEED EYE TRACKING

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MEG studies have shown that visual gradient stimuli elicit gamma band (30 – 70 Hz) oscillations in the human visual cortex. Correlated with the onset of visual motion, gamma band activity shifts towards a higher frequency range. Since the human visual system is tuned to capture movement of objects in the environment, changes in fixation elicited by the presence of the stimuli may underlie the visual gamma band shift. Eye-tracking systems have been previously used to exclude gross eye movements, blinking and large shifts in fixation, as the cause of drift in visual gamma oscillations. The recent introduction of MEG compatible high-resolution eye tracking systems facilitates the study of correlations between micro-saccadic eye movements and visual gamma activity. We conducted an MEG study utilizing a high-speed eye tracking system (EyeLink 1000, SR Research) to test the hypothesis that moving visual stimuli elicit increases in micro-saccadic eye movements as compared to baseline stationary conditions, and that this activity correlates with a shift in gamma oscillations. Six right-handed adult subjects were presented with a stationary vertical Gabor gradient at 0, 3, and 6 degrees horizontally from fixation. After a 1 second presentation, the gradient moved to the right for 2 seconds, motion was then reversed to the left for another 2 seconds. Based on eye tracking information, micro-saccades were quantified and trials were sorted based on prevalence of eye movements. Using this data, we will determine and present any existing correlations between increase of micro-saccadic movements and shifts in gamma oscillations. Additionally, this study demonstrates the validity of combining high-resolution eye tracking system with MEG measures of cortical gamma activity.

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P4-066

MONOCULAR LUMINANCE REDUCTION DECREASES DICHOPTIC PROCESSING IN PRIMARY VISUAL CORTEX

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Binocular interactions involve both excitatory and inhibitory interactions. The excitatory interaction depends not only on interocular signal strength but also on interocular timing. Little is known about the time dependence of the inhibitory interactions and where they occur. Mean luminosity changes can cause a delay in monocular responses: here we manipulate the interocular timing of responses by introducing an interocular luminance difference. We assess inhibitory binocular interactions by measuring dichoptic masking using MEG.

We presented two different flickering spatial noise stimuli at 4 and 6Hz in each eye respectively, to elicit a frequency-tagged steady state visual evoked response (SSVER) detectable in MEG traces. Then, we manipulated the luminance of the eye receiving the 6Hz stimuli with a 1.5ND neutral density filter and analyzed the power and dynamics of the response in V1. The ROI was defined from the fMRI retinotopic maps, all the MEG analyses were performed with Brainstorm.

In a monocular condition, we observed a phase delay and a decrease in the power of the response in V1 when the ND filter was applied. In the dichoptic masking condition, application of the filter to one eye dramatically decreased the contribution of that eye to the dichoptic response: it delayed and decreased the power of the response from the same eye more abruptly than in the monocular condition. In turn, it also greatly increased the power of response in the other eye compared to its dichoptic performance in the no-filter condition, therefore making it more dominant.

We conclude that temporal coincidence and the strengths of SSVERs are important markers of the inhibitory interactions underlying binocular vision in general, and dichoptic masking in particular. This dependence is seen in V1 responses and provides a basis for previous behavioral findings describing the decrease in binocular function induced by interocular luminance changes.

P4-067
MEG CORRELATES OF SACCADIC COMPETITION

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The saccadic distractor effect, in which irrelevant visual stimuli appearing opposite a target stimulus delay saccades to this target, is a popular tool for investigating saccadic competition. Recently, we showed how the temporal dynamics of this behavioral effect could be used to constrain crucial temporal parameters of a complex neuronal field model capturing the main properties of decision competition (Bompas and Sumner, 2011).

Here we test this framework using concurrent MEG and EOG recordings during a speeded saccadic orienting task to visual targets in the presence or absence of conflicting stimuli. 15 subjects were tested on four interleaved conditions: targets alone, distractors alone (requiring to keep fixation), simultaneous targets and distractors, and distractors presented 50 ms after the target.

Distractors presented alone often attract gaze automatically, resulting in errors. Distractors presented together with the target (SOA 0) also increase error rate while delaying all correct responses. In contrast, distractors appearing after the target (SOA 50ms) have little effect on direction but knock out a sub-population of saccadic latencies that would otherwise occur, producing a clear dip in the latency distribution.

These patterns of responses reflect the large variability between responses to identical experimental conditions. Here we address the origins of this unexplained variability by estimating, at each trial, the state of the perception-action network in the pre-target period, as well as the activity evoked by targets and distractors, to characterize their influence on subsequent saccadic response time and choice in humans.

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Reference: Bompas A, Sumner P (2011) Saccadic inhibition reveals the timing of automatic and voluntary signals in the human brain. Journal of Neuroscience 31:12501-12512.

P4-068
INVESTIGATING CROSSMODAL PLASTICITY IN BLIND INDIVIDUALS WITH MAGNETOENCEPHALOGRAPHY

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The study of blind individuals represents a unique model for investigating how experience drives the functional development of specific brain regions that are normally devoted to vision. It has been regularly demonstrated that occipital regions respond to sounds in congenitally and late-acquired blindness, even if to a lesser extend in the later group. One fundamental but unresolved question in the field relates to how non-visual information reaches the reorganized occipital cortex of blind individuals. Here we used magnetoencephalography to investigate the timing, strength and extent of crossmodal occipital activation in a group of congenitally blind (CB), a group of late blind (LB), and a control group of blindfolded sighted individuals. Participants were required to localize as quickly as possible if a sound was presented in the left or right side of space. The evoked-potential field analysis at the sensor levels evidenced stronger activation in the occipital sensors for blind individuals compared to controls peaking around 100 ms for CB and around 120 ms for LB. Source localization performed with LCMV beamforming technique in the 80-110 ms post-stimuli time-window evidenced the activation of an extrastriate occipital network for both CB and LB compared to controls with stronger activity for CB. Between 120 and 150 ms we observed bilateral occipital activity only in CB whereas a strong right temporo-parieto-occipital activation was observed in LB. These preliminary

results provide two important breakthroughs for our understanding of crossmodal plasticity mechanisms ensuing blindness: (1) sounds activate occipital regions in blind individuals at early post-stimuli timing, supporting a model of direct (feed-forward) connections between auditory and 'visual' regions; (2) the recruitment of occipital regions for auditory processing relies on different mechanisms according to the onset of blindness. Subsequent steps will consist in comparing the functional and effective connectivity in time-frequency domain for CB, LB and controls.

P4-069

OCCIPITAL BETA-BAND OSCILLATIONS REFLECT TARGET LOCATION AT MOVEMENT ONSET DURING A DELAYED POINTING TASK.

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Previous studies show that parietal regions encode movement goals in visual coordinates. It's also been shown that occipital neuromagnetic oscillations are modulated during delayed saccade tasks. We investigated the cortical dynamics subserving visuomotor transformations by recording neuromagnetic activity from 10 subjects while they performed delayed visual target pointing tasks. With the left eye occluded subjects fixated a central circle through a rectangular tube while a holster supported the pointing hand at midline. Three-dimensional movement of the finger was measured using an ultrasonic device (Zebris Medical,GmbH). Peripheral targets were presented for 250ms to left or right of fixation at horizontal eccentricities between 9^0 and 20^0. After a delay period of 1–1.5s the fixation changed in hue signaling a cue to point either at the remembered target location (PRO) or at the analogous location in the opposite hemi-field (ANTI). In a third condition, the lens of the viewing apparatus was replaced by a left-right reversing prism. After a short training period, subjects were instructed to point to the location of the remembered target (PRISM). MEG data was analyzed using a Matlab based beamformer source analysis tool (BrainWave). Event-related modulation of the alpha-and beta-bands within a posterior region-of-interest was evaluated during a 400ms window centered on the centrally presented cue-to-move stimulus. The results show that at the time just preceding movement onset a lateralized beta-desynchronization occurs in occipital cortex that is consistent with the previously presented target location. This effect occurred independent of movement direction (i.e. even when visual direction was dissociated from movement direction in the anti and prisms tasks), suggesting a reactivation of the retinal impression just prior to initiation of movement. These results support a role for occipital cortex and visual-based coordinate systems during visuomotor transformations.

P4-070

FUSIFORM GYRUS ACTIVATION FOR GAZE CONTACT: AN MEG/EEG ANALYSIS.

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Eye gaze is a foremost social cue in human communication. In particular, gaze contact has acquired a high social significance; it constitutes the most basic form of interpersonal contact and a frequent preliminary to social interaction. Accordingly, there is evidence for faster detection of gaze contact than averted gaze and for better memory encoding of faces with eyes directed at us than for faces with averted gaze. Brain imaging studies showed enhanced fusiform cortex activation to faces with direct gaze (George et al., 2001). Yet, whether this reflects early modulation of face-related perceptual activities remains unclear, particularly because modulations of the electrophysiological marker of face perception, the N170 in EEG and the M170 in MEG, have been reported in different directions in relation with direct and averted gazes (e.g. Conty et al., 2007; Puce et al., 2000). Using MEG/EEG, we here explored the brain responses to faces with direct and averted gaze as used by George et al. (2001). Twelve subjects were recorded in MEG (151 channels whole-head CTF system) and EEG (64 amagnetic channels). We found enhanced N170 in response to direct than averted gaze faces in the right hemisphere, while the M170 peak was larger for direct gaze but only under the face deviated head views. Using source reconstruction of the MEG data based on a weighted minimum norm estimate (wMNE), we demonstrated that these electromagnetic modulations were explained by stronger activity from the right fusiform gyrus to direct than averted gaze under deviated head views between 145 and 165 ms. Additional activations were observed in the right occipital gyrus, the bilateral precentral gyri, the left superior parietal lobule and the right middle cingulate cortex. These results suggest that direct gaze increases the early perceptual encoding of faces and modulates the attentional network.

P4-071

VISUAL EVOKED MAGNETIC FIELDS ELICITED BY CHECKERBOARD PATTERN-ONSET STIMULATION

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This magnetoencephalography study investigated the cortical origins of the visual evoked response elicited by checkerboard pattern-onset stimulation.

Visual stimulation consisted of a 10x10 black and white checkerboard pattern (pattern-onset) and a uniform gray pattern (pattern-offset) alternating at 500-ms intervals. The luminance of the patterns was 260 cd/m2 for the white squares and 6.0 cd/m2 for the black squares, and 132 cd/m2 for the

gray pattern. Therefore, the mean luminance of the stimulation pattern was constant with time. Left or right half visual field stimulations were presented to the dominant right eye of seven normal subjects. Visual evoked magnetic fields were measured with a 306-channel magnetometer (Vectorview, Neuromag) in a darkened magnetically shielded room.

The evoked magnetic field contour map for the primary component showed a contralateral single vertical current dipole pattern at around 90 ms (CI) in four subjects, and a contralateral single horizontal current dipole pattern at around 100 ms (prolonged N75) in two subjects. No P100 wave was observed. Source localization using a single current dipole model estimated the CI source in the parieto-occipital sulcus (V5), and the prolonged N75 source in the calcarine fissure (V1).

This study suggests that the visual evoked response elicited by checkerboard pattern-onset stimulation is generated through the achromatic dorsal visual pathway (M-pathway), with simultaneous activations in the higher visual cortices and the primary visual cortex.

P4-072

NEURAL BASIS OF READING JAPANESE KANJI AND KANA IN THE LEFT FUSIFORM GYRUS: AN MEG STUDY

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Japanese writing system uses two different scripts: Kanji (ideograms) and Kana (phonograms). Our recent ERP and fMRI studies (Neurosci Res, 2012; NeuroImage, 2012) demonstrated the differential roles of spatial frequency (SF) on reading Kanji and Kana; high-SF for Kanji and low-SF for Kana. Pure alexia for Kanji is caused by the lesion of left mid-fusiform gyrus (FG), whereas the impairment of left posterior FG induces pure alexia for Kana. However, it remains unknown how Kanji and Kana are differently processed in the left FG. To elucidate this issue, neuromagnetic responses to unfiltered and spatially-filtered (high-SF, low-SF) word stimuli were recorded with a 306-ch MEG system in eight healthy native Japanese. Word stimuli included early- or late-learned Kanji (EKj, LKj) and Kana word or non-word (KaW, KaN). Region of interest (ROI) for left FG was imported from brain annotation provided by FreeSurfer. The peak-latency and amplitude of major component (N170m) were estimated by visual inspection using the sensor detection. The source localization results were obtained using minimum norm estimates for individual data first and then transformed into the standard brain (MNI305) for the group analysis. The coordinates of the peak activities in ROI across the subjects were also estimated. The N170m latencies for KaW and KaN were significantly shorter than those of LKj and EKj under the unfiltered condition. However, the estimated peak coordinates of N170m were almost identical between Kanji and Kana, even in more contrastive comparison between high-SF-LKj and low-SF-KaW. These findings indicate that the brain regions for processing Kanji and Kana are relatively overlapping within the left FG despite the faster processing speed of Kana. Therefore, we consider that the different causative lesions of pure alexia between Kanji and Kana are linked to the distinct brain network via the left FG but not the left FG itself.

P4-073

READOUT OF DYNAMIC ACTION SEQUENCES WITH MEG DECODING

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The human brain can rapidly parse a constant stream of visual input. The majority of visual neuroscience studies, however, focus on responses to static, still-frame images. Here we study the dynamics of visual processing of videos using MEG decoding analysis (also known as MVPA or readout). MEG provides an optimal tool for studying this problem, due to its high temporal resolution. In this study, subjects viewed a series of videos of different actors performing different actions (e.g. run, walk, jump) under different transformations (e.g. viewpoint, speed of execution) while in the MEG. In order to assess the amount of stimulus information in the neural signals, we decoded which action the subject was viewing based on their MEG data at each time point. Action identity can be decoded with above chance accuracy during the period of 300-700 ms after stimulus onset. Both decoding accuracy and human behavioral performance are significantly lower when motion coherence is disrupted. These results show that even with form information preserved, a lack of motion coherence negatively impacts action recognition, and this impairment can be detected in the decoded MEG signals. Finally, we developed a computational model that agrees with these MEG data. Based on these results, we propose a biologically plausible computational procedure to recognize actions across complex transformations. This study highlights MEG decoding as a useful tool for studying visual processing of videos.

P4-074

INTERACTION BETWEEN THE DORSAL AND VENTRAL VISUAL SUBSYSTEMS WHILE PERCEIVING 3-D OBJECT SHAPE FROM 2-D MOTION: AN MEG-FMRI STUDY

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We used both MEG and fMRI to visualize the dynamic brain responses to 3-D object perception from random-dot motion. Also, we employed

causality analysis to infer driving relationships between the neural activities along the two visual pathways.

The visual stimuli consisted of 1000 random dots whose motion coherence was manipulated parametrically to create different levels of 3D perception and to study the associated changes in brain activity. MEG signals were measured using a 306-channel MEG system and fMRI data were collected using a 3-Tesla scanner with the single-shot EPI sequence. The results of the block-design fMRI data were used to impose plausible constraints on the MEG inverse calculation using a weighted minimum-norm approach. In order to test the directional influences between the active regions detected in the spatiotemporal activity estimates, Granger causality was calculated on the raw MEG time-series extracted from ROIs where significant activities were observed in the MEG-fMRI analysis.

The results showed that the activities in the posterior inferotemporal (pIT), the parietooccipital (PO), and intraparietal (IP) regions were increased at different latencies during highly coherent motion conditions in which subjects perceived robust 3D objects. The interactions inferred by the Granger causality showed that there were significant directional influences from MT to PO, IP to pIT, and pIT to PO only in the conditions where robust 3D objects were perceived.

The results indicate that these regions were involved in a large-scale neural network underlying the perception of 3-D object structure from 2-D motion. The results also support the idea that PO, which was investigated in detail in the previous fMRI studies on 3-D SFM, receives feedback input from pIT as well as feedforward input from MT to form robust 3-D percept by integrating the global motion and the object information processed in the ventral visual system.

P4-075
TIMING OF CORTICAL ACTIVATION IN GRAPHEME-COLOUR SYNAESTHETES REVEALED THROUGH INDEPENDENT COMPONENT ANALYSIS IN THE MEG

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Grapheme-colour synaesthetes experience an anomalous form of perception in which graphemes systematically induce specific colour concurrents in their mind's eye ("associator" type). Although it has been well characterized behaviourally, its neural mechanisms remain unresolved. There are currently two competing models: while the first (Cross-Activation) posits early recruitment of occipital colour areas in the initial feed-forward sweep of brain activity, the second (Disinhibited Feedback) posits later involvement of a multisensory convergence zone (for example, in parietal cortices) after graphemes have been processed in their entirety, and subsequent feedback to early visual areas (i.e., occipital colour areas).

We have here conducted an MEG study on associator grapheme-colour synaesthetes (n=6) using Independent Component Analysis (ICA) on a single-subject level to decompose the acquired signal and identify the dominant patterns of the induced, synaesthetic experience. Since the timing and cortical areas underlying the induced, synaesthetic percept are still very much under debate, and since no "synaesthetic" event-related components have been confirmed, ICA is an ideal method for extracting the patterns of brain activity consistently present across trials in individual grapheme-colour synaesthetes.

We do not find early, evoked activity in visual areas that dissociates between presentation of synaesthesia-inducing letters and non-inducing symbols. Rather, our single-subject ICA analysis reveals evoked activity that significantly dissociates between these two conditions at approximately 190 ms following grapheme presentation. This effect is present in grapheme-colour synaesthetes, but not in matched controls, and exhibits an occipito-parietal topology localised consistently across individuals, via a Minimum Norm inverse solution, to extrastriate visual cortices, as well as to superior parietal lobules. Due to the late timing of this evoked activity and its localisation, our results provide evidence against a Cross-Activation model of synaesthesia, and rather support a Disinhibited Feedback model, at least in our sample of associator synaesthetes.

P4-076
NEURAL OSCILLATORY DYNAMICS UNDERLYING TEMPORAL RECALIBRATION DURING MULTISENSORY INTEGRATION

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Combining sensory information across the senses can markedly improve perception. Audiovisual signals are a particular common cross-sensory pairing; their different physical and physiological transduction times, however, make optimal integration difficult to achieve. Temporal recalibration perceptually realigns inputs between the senses: exposure to a given audiovisual asynchrony will cause similar asynchronies to appear less pronounced than before. Temporal recalibration occurs rapidly, contingent upon the asynchrony on the preceding trial. It is unclear, however, how such rapid cross-modal recalibration is achieved.

An increasing body of evidence demonstrates that the amplitude of a high frequency oscillation is systematically modulated during the course of a low-frequency cycle (phase-amplitude coupling, PAC). PAC has been suggested to facilitate the transient coordination of local networks on short time scales and integrate multiple networks in disparate locations across longer time scales. PAC is therefore a candidate mechanism underlying temporal integration across the senses. In order to investigate these complex neural oscillatory dynamics for temporal recalibration, we used brain imaging with magnetoencephalography (MEG) in healthy human subjects engaged in an audiovisual integration task. On each trial, subjects judged whether an audiovisual stimulus pair of varying stimulus onset asynchrony (SOA) was synchronous or not.

Our results show that on average participants recalibrated their simultaneity perception by 35 ms. Analysis of PAC revealed concurrent shifts of the high frequency oscillatory component of PAC in the visual cortex. Importantly, the subjects' individual temporal recalibration estimates were significantly correlated with the magnitude of these shifts. These findings suggest that dynamic

changes in the interaction between oscillations of different frequencies is critically involved in the neural mechanisms underlying temporal recalibration.

P4-077

SPATIOTEMPORAL ANALYSIS OF HUMAN FACE INDIVIDUATION

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The perception of human face identity relies on a distributed network consisting of multiple brain areas, particularly within occipital and ventral temporal cortex. However, the spatiotemporal dynamics of information flow among these regions in service of individual-level face processing is unknown. In this study, images from different faces were presented to human subjects while using MEG to record their brain activity. The faces were shown with multiple facial expressions to allow us to examine face individuation processing invariant over expression. After reconstructing the source space signals, we used a spatiotemporal searchlight algorithm to search through the neighborhood of each source voxel and applied multivariate pattern classification to decode the spatiotemporal progression of face identity information. Using multivariate statistics and permutation testing, we identified the statistical 'hotspots' of face individuation in space and time. The results show that multiple brain areas along the ventral visual stream, including occipital face area (OFA), fusiform face area (FFA) and the anterior inferotemporal cortex (IT), are involved in expression invariant face individuation. The spatiotemporal distribution of the face-individuation 'hotspots' suggests that there is a posterior to anterior flow of face-individuation information. Specifically, classification accuracy becomes significant in early visual cortex around 90 ms after the stimulus onset. OFA and FFA show peak classification of individual face at around 200-250 ms. Classification of individual faces peaks after 250 ms in anterior IT areas. These results elucidate the posterior-to-anterior flow of information that underpins our ability to individuate and recognize faces.

P4-078

TEMPORAL DYNAMICS IN FEAR CONDITIONING

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Pavlovian conditioning has extensively been used as experimental model to study fear. PET and fMRI studies have outlined some fear-relevant brain regions, as well as functional connections between them and deeper limbic structures. However, the sluggish BOLD response is unlikely to capture the full spatio-temporal dynamics of fear conditioning might. In the present study we used MEG to add to the overall picture by focusing in particular on oscillatory responses. Twenty healthy right-handed adults (10 females; age: 28.05 ± 3.3 years) participated in the experiment. Two fearful faces were used as conditioned stimuli (CS+ and CS-) flickering at 15 Hz for 5 seconds. The unconditioned stimulus (US) was an unpleasant electrical stimulation at the left median nerve. Induced oscillatory activity was calculated on sensor level and source analysis (Dynamical Imaging of Coherent Sources, DICS). Statistics on sensor level were estimated via a nonparametric permutation test, while on the source level a minimum number of voxels was determined through 3dClusterSim.

Results revealed a negative cluster in the alpha and beta band, marking reductions during CS+. Its early component involved mainly the alpha range and was localized to secondary visual areas. The later difference involved two regions centered on right putamen and middle frontal gyrus for the alpha and beta band respectively. Post central gyrus contralateral to the upcoming US exhibited also reduced power in these two frequency bands.

Our findings relate fear conditioning to enhanced excitability at sensory regions, like visual and somatosensory cortices, as well as putamen. The latter structure has been related to various types of learning. In conclusion, temporal dynamics of fear conditioning involve certain cortical and deeper brain structures indicating the activation of a distributed functional network.

P4-079

AROUSAL AND VALENCE INFLUENCE ON SPATIOTEMPORAL PATTERNS OF BRAIN ACTIVITY ELICITED BY VISUAL AFFECTIVE STIMULI

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Emotional states evolve in a trajectory that spans at least two independent dimensions, arousal and valence. We hypothesize that arousal and valence are encoded via unified mechanisms that recruit distinct neural circuits of cortical and subcortical regions. We tested the quantitative consequences of this hypothesis by mapping the spatiotemporal profile of evoked brain responses elicited by stimuli with distinct and well-defined levels of arousal and valence. Magnetic fields were recorded from ten healthy adult individuals passively viewing affective pictures rated along arousal and valence. A beamformer technique was used to identify changes in regional activations elicited by the emotional stimuli across time within the gamma band. The results showed that high arousal elicited increases in activity in the temporal pole, the frontal gyrus, the temporal gyrus and the lingual gyrus. Regions responding differentially to valence included the frontal gyrus (higher for pleasant) and the occipital gyrus, the precuneus and caudate nucleus (higher for unpleasant). Distinct arousal-by-valence interactions were present in frontal and gyrus rectus, caudate nucleus and putamen (arousing-pleasant), and in superior parietal gyrus (arousing-unpleasant). The temporal profile of the responses showed that: (i) arousal and valence were encoded in parallel within several cortical and subcortical sources, (ii) valence encoding was prioritized

to all other effects (onset at 40 ms), (iii) pleasant valence was short lived in comparison to unpleasant valence (offsets at 90 and 320 ms respectively), and (iv) arousal-by-valence interactions may reflect a behavior that maximizes exposure to arousing pleasant events and minimizes exposure to arousing unpleasant events; thus, pleasant and high arousal encoding results in slower encoding times.

P4-080

PREDICTIVE AMBIGUITY OF PERCEPTION IN THE PRE-STIMULUS WINDOW

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Figure-ground illusions create an ambiguous and bistable perception even though the retinal information is constant. In the case of the Rubin's vase figure the interpretation of the stimulus as being either a pair of face or a vase are in a perpetual competition, with perceptual reports of participants fluctuating over time. Within this present study we used this phenomenon as a conduit to understand the predictive nature of oscillatory brain activity, and its resultant impact upon perception. Specifically we predicted that pre-stimulus low-frequency spontaneous oscillatory activity would contribute to a brain state that biases the upcoming dominant percept generated by the stimulus. To this end we conducted an MEG experiment whereby participants were presented with the Rubin's vase figure for a brief period (150msec), and asked to report if they saw either a vase or a face. Contrasting the pre-stimulus periods of both reports, we found increased low-frequency power (12-17Hz) when participants' subsequently reported a face. This effect was localized to right lateral occipital cortex (LOC), an area frequently implicated in object perception. In line with the notion of alpha inhibitory gating, these data suggests that in the case of the competing interpretations of the stimulus, that object processing is subdued. This results in a relative boost of processing of facial features that bias perception towards the face. In order to follow up, we will investigate the global dynamics of the perceptual processes, to ascertain how this local signal alters the systems state of information flow.

P4-081

UNIDIRECTIONAL DYNAMIC CONNECTIVITY FROM SUPERIOR PARIETAL LOBULE TO FRONTAL EYE FIELD IMPLEMENTS SPATIAL ATTENTION SHIFT IN A COMPLEX VISUAL MOTION SEARCH TASK

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Attention shifts are an integral component of detecting goal-driven features in complex visual-spatial tasks. Previous fMRI and MEG studies have shown the importance of the Superior Parietal Lobule (SPL) and Frontal Eye Field (FEF) in the endogenous spatial attention shift. Here we characterize the interaction between SPL and FEF by computing measures of association from MEG data obtained from a complex visual motion search (VS) task. The VS stimulus consisted of 9 moving spheres, 8 simulated the forward translation of the observer and one sphere (the target) moved independently, with a different speed and/or direction (forward or backward). At the end of motion, 4 of the spheres were labeled, one of them being the target. Eight young, healthy subjects were studied. Responses were entered with the right hand via button press on an MEG compatible button box. The subjects maintained fixation at the center of the display and trials with eye movements were discarded during data analysis. In our previous MEG study of spectrotemporal power in this task we found an attention modulating fronto-parietal network (MPFC-SPL-FEF) synchronized in the 10Hz alpha-band and that SPL and FEF were highly sensitive to target location suggesting their role in attention shifting. To better understand the latter finding , we used here dynamic Granger Causality (DGC) connectivity between SPL and FEF to compute the timing and directionality of their communication in the VS task. There was forward connectivity from SPL to FEF in both the left and right hemispheres but no backward connectivity. As expected, this pattern of connectivity was not present in a typical self-motion task where there was no independently moving object. Our results suggest that SPL may be involved in deciding "where" to shift spatial attention and sends this information to FEF which actually performs the endogenous shift of attention.

P4-082

MAPPING THE CONTRAST TUNING FUNCTION OF THE VISUAL GAMMA RESPONSE USING A CONTINUOUSLY-VARYING STIMULUS

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Oscillatory responses to visual stimulation in the gamma frequency range have been the subject of intense interest in the field of visual neurophysiology for many years now. Traditionally, the process of mapping the tuning function of the gamma response to stimulus parameters such as contrast has been achieved by using a number of discrete conditions in which stimuli are presented at a fixed parameter level in each condition. Here we investigated a more efficient approach in which the parameter of interest is varied continuously, and the corresponding modulation of the gamma response with respect to time can then be used to infer the tuning function. Thus, we recorded data from 18 participants using a 275 channel CTF MEG system, while they viewed a circular grating stimulus that varied between 41-100% according to a triangular waveform with period 4.5s. The gamma-band response (30-70Hz) was source-localised to occipital cortex using the SAM beamformer. A virtual electrode analysis was performed at the location of maximal statistical difference between baseline and stimulation,

and spectrograms of the induced response were then calculated using the Hilbert transform. By measuring changes to the amplitude and frequency of the visual response with respect to changing stimulus contrast over time we were able to determine the contrast tuning function of both parameters. Consistently, across participants we found that both amplitude and frequency increased linearly with stimulus contrast, consistent with recent animal LFP work [1], but that the slope of this function varied considerably across individuals. This variability in the gain of the response with respect to stimulus contrast may partially explain the apparent variability in the strength of the gamma response across individuals in studies in which a fixed contrast stimulus is used.

[1] Ray S., & Maunsell JHR. (2010). Neuron, 67(5), 885–896.

P4-083

SIMULTANEOUS MEG-INTRACRANIAL EEG REVEALS THALAMOCORTICAL SYNCHRONIZATION DURING HUMAN VISUAL PERCEPTION

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The thalamus not only passively relays information to the cortex, but actively processes and modifies it (Saalmann & Kastner, 2011). Thereby, information between the thalamus and the cortex is transferred via recurrent thalamocortical loops (Theyel et al., 2010). Recent work in monkeys suggests that the thalamus modulates cortical alpha activity during visual processing (Saalmann et al., 2012). Evidence from humans, however, is lacking.

We simultaneously recorded intracranial EEG and MEG in six epileptic patients implanted with depth electrodes for deep brain stimulation therapy. The patients performed a discrimination task, during which they were instructed to recognize near-threshold, masked visual stimuli. As a measure of thalamocortical communication, phase synchrony between thalamic electrodes and MEG sensors was analyzed (phase-locking value). We identified a pronounced increase in phase synchrony between thalamic depth electrodes and MEG sensors in the alpha band (7-12 Hz). Perception performance was predicted by a frequency shift in alpha phase synchronization prior to the stimulus onset. Localizing thalamocortical coherence (DICS beamformer) revealed a network of sources including parietal brain regions.

The study provides first evidence from simultaneous intracranial and MEG recordings in humans, highlighting the importance of thalamocortical communication for visual perception. Phase synchronization between the thalamus and the cortex in the alpha band predicted perception performance, which is in line with previous work in monkeys (Saalmann et al., 2012) and consistent with recent frameworks on human perception and attention (Jensen et al., 2012; Hanslmayr et al., 2011). The speeding of thalamocortical phase synchrony prior to perceived stimuli potentially reflects increased states of arousal (Hughes et al., 2004), during which thalamic activity speeds up cortical processing.

P4-084

DECODING OBSERVED ACTIONS FROM BRAIN OSCILLATIONS: A MULTIVARIATE PATTERN MEG STUDY

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When we observe other people's actions, we recruit similar frontal areas that are also recruited when we perform actions ourselves. Such findings have been taken to support the view that in order to understand an action, we simulate that action in our own motor system. Alternatively, it has been argued that actions are understood on the basis of a perceptual analysis, with access to action knowledge stored in the conceptual system. Here we investigated at which point in time and in which brain regions it is possible to distinguish between two different observed actions (pointing, grasping), irrespective of the direction (left, right) and the effector (left hand, right hand).

We used magnetoencephalography to measure brain activity of 17 participants watching short videos of hand actions (pointing, grasping) to the left or right side using either the left or the right hand. Univariate time-frequency analysis showed a significantly stronger desynchronization in the beta-band for grasping than pointing in a cluster over right sensorimotor sensors towards the end of the video, around the time when the hand touched the object. To identify the positions in frequency, time and sensor space that distinguished the two actions while generalizing across direction and effector, we ran a cross-conditional multivariate searchlight analysis. We found that the two observed movements can be distinguished at an earlier stage of the video in the theta- and low alpha-bands. Source analysis indicated that the difference obtained in the high alpha- and beta-bands was mainly located in frontal and parietal regions, while the earlier difference observed in the theta- and low-alpha bands was mainly located in bilateral temporal regions.

Our results suggest that temporal regions have access to abstract action representations earlier than frontal regions, providing important constraints for biologically plausible models of action understanding.

P4-085

NEUROMAGNETIC CORRELATES OF ACTION PROBABILITIES AT DIFFERENT HIERARCHICAL LEVELS DURING ACTION OBSERVATION

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Predictive coding has been put forward as a general principle underlying neural processes. In this view, the brain's main function is to reduce prediction error. Although the power of the concept lies in its generalized

applicability, i.e. to multiple levels of processing, the majority of experimental evidence has been obtained only from low-level sensory systems.

Here we investigated if the predictive processing mechanism generalizes to the action domain, by examining the neural correlates of prediction errors both at the action kinematics and the action outcome level, in an action observation task using magnetoencephalography (275-channel CTF MEG-system, Coquitlam, Canada). 24 healthy participants viewed animated videos of a bowler throwing a ball down a bowling alley. We manipulated the probabilities of action kinematics (ball direction: towards left, center, or right) and action outcome (3, 6, or 9 pins hit), with three frequencies of occurrence per component (10%, 30%, or 60%). To ensure participants remained attentive, they had to answer a question about either the ball direction or the number of pins that were thrown over, after each fifth trial (on average). Subjects first practiced for 30 minutes before they went into the MEG, to allow them to internalize the conditions' probabilities.

Our hypothesis was that conditions that would occur least frequently would lead to high prediction errors, and vice versa, and that this prediction error modulation would be reflected in the strength of the oscillatory components in the MEG-signal. Data were analyzed using FieldTrip/Matlab, and data time courses were reconstructed using beamforming techniques, in both the action observation (action kinematics) and mentalizing (action outcome) networks. We explored evidence suggesting that the power in the alpha/beta-range in both regions is consistently modulated by the conditions' probabilities, which would imply that the predictive coding mechanism also underlies neural activity related to higher-order cognitive processes.

P4-086
FEATURE CODING IN FACIAL EMOTIONS FROM MEG DATA

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Emotional face processing is ideal to examine task specific encoding of highly salient natural visual categories (facial expressions of emotion), where observers make accurate and rapid decisions based on a small set of known diagnostic features (Schyns et al., 2007).

We recorded 21,000 trials of MEG data per observer (n = 5) performing a forced choice task on the examples of the seven basic expressions. On each trial, we randomly sampled Gaussian 'bubbles' of image space at five different spatial frequency bands, restricting observers to 75% accuracy (Gosselin & Schyns, 2001).

For each observer we performed Independent Components Analysis on the MEG data. For each ICA component and expression, computed Mutual Information to between pixel visibility and the MEG signal response (every 2 ms, bandpass filtered 1-40Hz). This creates a movie of 500 Mutual Information images (+/- 500ms around stimulus onset) representing the total sensitivity of the MEG signal to facial expressions of emotion. We performed Non-negative Matrix Factorization (NMF) on this image set across expressions, deriving a common, parsimonious parts-based representation of face regions that modulate brain activity.

We computed the coding dynamics of components. Per trial, we correlated the sample of stimulus information (pixel-wise) with each NMF part, quantifying the strength of this feature-part in the stimulus. For each time point we compute MI between single-trial feature strength and component amplitude. The contralateral eye is encoded early, but dominates only initially (150ms post stimulus). Each subject shows at least one (Left or right occipital/fusiform) components, maximally sensitive to multiple mid SF band face features (100-200ms post stimulus) independent of expressions. Expression specific components develop sensitivity in the same period but show a slower and later transition between features (e.g. right eye to mouth in surprise) or within features (e.g. left to right mouth in happy).

P4-087
DOES TRANSCRANIAL MAGNETIC STIMULATION OF VISUAL CORTEX AFFECT THE RETINA?

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Clearly, the retina transfers massive amounts of information to the cerebral cortex. In some animals, the cerebral cortex has been shown to conversely modulate retinal activity via efferent connections. However, whether such connections exist in primates, and whether visual cortex could transmit information back to the retina, remains controversial yet relatively unexplored.

We therefore used transcranial magnetic stimulation (TMS) of visual cortex to stimulate any potential efferent pathways to the retina. Phosphenes were evoked by single pulse stimulation applied over left and right visual cortex, guided by MRI-based neuronavigation. The electrical activity of the retina (electroretinogram, ERG) was measured with DTL fiber electrodes on both eyes, while eye movements were monitored using horizontal and vertical electrooculography. Data processing included removal of the consistent TMS pulse artifact, and rejection of subsequent TMS artifacts, saccades, and blinks by visual inspection. Both TMS-evoked potentials and time-frequency representations were computed.

In response to the TMS pulse, the ERG electrode contralateral to the stimulation site recorded high-frequency activity from 80 to 100 Hz and from 200 to 330 Hz centered around 50 ms. For the ipsilateral eye, an increase in activity from 150 to 300 Hz occurred in the same time range. Additionally, the evoked potential contained a slower positive potential from 70 ms to 100 ms, post-stimulus, for the ipsilateral eye. The morphology and topography of these results appear distinct from classic artifacts from eye movements, blink artifacts, or facial muscles, though further work must be done to rule out more subtle effects from these sources. However, replication of the experimental procedure with a conductive phantom ruled out the possibility of interference originating from the TMS device itself.

The results suggest that magnetic stimulation of visual cortex may induce retinal responses, which would provide evidence for a corticoretinal pathway.

P4-088
VISUAL STIMULI EVOKE RETINAL RESPONSES DETECTABLE WITH MEG

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We investigated the ability of whole-head magnetoencephalography (MEG) systems to detect retinal activity. Electroretinogram (ERG) activity was measured from the right eye with a DTL fiber electrode simultaneously with MEG. Brief white flashes were presented with either the left or right eye covered in separate blocks.

A cluster permutation method based on factor analysis and independent component analysis was developed to identify MEG lead field components synchronous with the ERG b-wave (the largest evoked potential feature in the retina, with a latency of ~50 ms).

Topographic maps of extracted lead field components from the left-eye-covered condition show coherence from right-frontal sensors, along with an occipital component that may reflect a synchronous visual cortical response. To verify that this source was not a result of the ERG apparatus contaminating the MEG, the right-eye-covered condition was also examined. The left eye was not measured with an ERG electrode, so the right-ERG waveform was used to extract the lead field components with the factor analysis method. Topographic maps of the extracted lead fields showed coherence from left frontal sensors and occipital sensors. The polarity of the frontal sensors was flipped between stimulation of the left and right eyes, consistent with previous reports of the magnetoretinogram.

Beamformer analysis using the isolated frontal lead field components reconstruct sources in the uncovered eyeball, with morphology similar to the ERG and a anterior-posterior dipole orientation. This is consistent with the orientation of the retinal generators of the ERG, which are aligned radially with respect to the eyeball surface. However, with a typical head model, and inclusion of only cerebral cortex in the reconstruction, these sources were apparently mislocalized to the anterior temporal lobe.

We therefore demonstrated that retinal activity can be extracted from MEG data, but may sometimes be inadvertently confused with anterior temporal lobe activity.

P4-089
BIOMAGNETIC RESONANCE IMAGING

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As a “New and emerging techniques” of Biomag2014, I would like to introduce a possible research field, “biomagnetic resonance imaging”, in biomagnetism. The research field could cover studying brain functions, heart function, etc.

For example, as an application for brains, I present an idea, brainwave magnetic resonance (BMR), for direct imaging of the brain functional connectivity by matching the NMR frequency to the frequency of a periodic neural oscillation like alpha- or gamma-band waves. Technically, such a low frequency NMR signal can be detected by SQUID-based micro-Tesla MRI technology. The feasibility of BMR was demonstrated by localizing closely-placed correlated current dipole sources with a multi-dipole brain phantom, which had been quite tricky with other developed modalities like EEG or MEG [1].

The biomagnetic resonance imaging is not only limited to the brain wave measurement but also extending to the measurement of any kind of periodically-oscillating electrophysiological activity like pathological reentry excitation in brain cortex or myocardium [2].

I hope the suggestion of this research topic could stimulate novel pragmatic measurement ideas in the biomagnetism research society.

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P4-090
OPTIMIZATION OF MINIMUM-NORM ESTIMATE (MNE) OF CORTICAL SOURCES USING A SENSOR-SPACE TASK-RELATED INFORMATIONAL CONTENT METRICS FOR NOISE MODELLING

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Introduction: Cortical sources are well reconstructed from MEG input signals with high information content (high signal-noise ratio) as evoked potentials. In case of weak brain activities, as imaginary motor task related brain activity, source reconstruction fails to provide convergent mathematical solution. Several studies have already reported introduction of a priori hypotheses from fMRI into source space for source reconstruction. We propose a method introducing information in the sensor space.

Materials and methods: From MEG/EEG recordings, informational content in the sensor space is assessed by multivariate correlation in the time window corresponding to the task performance or by quantifying signal entropy. The sensor space noise model is dynamically updated by covariance matrix adjustment using correlation or entropy data. This dynamic noise model is exploited using standard MNE source reconstruction algorithm. This optimized MNE algorithm has been applied to MEG recordings averaged trials during real and imaginary motor tasks in 10 subjects.

Results: Compared to standard MNE source localization in real motor tasks, our method resulted in more contrasted and more focused sources.

Applied to imaginary motor tasks, our method led to more salient activation patterns allowing for a better discrimination between tasks.

Conclusion: Dynamic noise modelling using sensor-space task related information allows for a better source reconstruction when the informative content of input signals is low.

P4-091
ROTATIONAL INVARIANCE AND SOURCE ORIENTATION IN LCMV VECTOR BEAMFORMER

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The linearly constrained minimum variance beamformer is an adaptive spatial filter commonly used to solve the inverse problem in MEG, that is to determine the neuronal activity at the source of the detected magnetic field surrounding the head. This is done by finding an optimal linear combination of the sensors (weights vector) to represent each possible source location and orientation, such that the power from other locations and orientations is minimized, while maintaining the desired source amplitude by an appropriate choice of linear constraints. In the scalar beamformer approach, a single weights vector is obtained, corresponding to an “optimal” source orientation, for each source location. In the vector approach, two or three orthogonal source orientations are kept at each location and typically their resulting power is summed.

Unfortunately, some commonly used vector beamformer constraints are not rotationally invariant, meaning that the results will depend on the orientation of the physical coordinate system. Some of these formulations are meant to correspond to well-known scalar constraints and can be seen in most cases as a sub-optimal solution, adding a minor distortion in the reconstructed activity that can affect amplitude as well as localization. On the other hand some recommendations suffer from extreme effects; for example the idea of adding scalar solutions in orthogonal directions instead of using a vector formulation would only detect sources oriented almost exactly along the coordinate axes.

We suggest rotationally invariant constraints for the vector beamformer and compare the resulting solutions with other vector and scalar options. In particular we extend previous work investigating localization bias, and also consider angular bias. We hope this work will offer insight into the scalar and vector beamformers, the issue of selecting or measuring source orientation, as well as allowing authors of analysis tools to verify and easily correct non-rotationally invariant implementations.

P4-092
SENSITIVITY OF MEG/EEG SOURCE RECONSTRUCTION TO CONDUCTIVITIES OF COMPACT AND CANCELLOUS BONE IN THE PRESENCE OF SKULL DEFECTS

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The influence of skull defects on the MEG and EEG signals recorded above the skull defects was recently determined to be substantial using an in vivo animal experiment [1]. Our objective is to determine the influence of compact and cancellous bone layer conductivities on MEG and EEG source reconstruction in the presence of skull defects.

We constructed a complete finite element (FE) simulation of an in-vivo animal experiment with a skull defect above a controlled source [1]. The body, ocular humour and lens, compact and cancellous bone, skull defects and grey matter, white matter, CSF and intracranial blood vessels were segmented from a T2 MRI (0.4 mm3) and a co-registered CT (0.4 mm3). A nodeshifted cubic mesh was derived (Vgrid). Source reconstruction from the EEG and the MEG recordings respectively was performed using an unconstrained moving dipole fit (SimBio). The conductivity of compact and cancellous bone in the FE model was varied by ±50%, ±20% and ±10%.

In the reconstruction from MEG signals, the influence of cancellous bone conductivity on the equivalent source position was stronger in the presence of skull defects than without skull defects. In the reconstruction from EEG signals, the compact bone conductivity influenced the source reconstruction error due to ignoring a skull defect. In this model, very low compact bone conductivity (-50%) displaced the equivalent sources from the grey matter into the skull defect and cancellous bone volume.

In the presence of post-surgical skull defects, compact and cancellous bone should be differentiated in the FE head model and their conductivities carefully determined, because the conducting defect tissue allows the volume currents to extend farther into the cancellous bone layer. Accurate FE method based head modelling incorporating skull defects can improve localisation of brain activity.

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P4-093
FLEXIBLE HEAD-CASTS FOR HIGH SPATIAL PRECISION MEG

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To minimize uncertainty in head position we recently presented a technique that used 3D printing to make headcasts that fit the surface of the head (internally) and the inside of the MEG dewar (externally) (Troebinger et al, 2014). These solid headcasts gave excellent precision but covered the subjects’ eyes and were rather intimidating to wear. Here we present a new headcast prototype made of flexible polyurethane foam which leaves the eyes uncovered. This considerably enhances the comfort and ease of use

of these devices. The casts are constructed with indentations to house the fiducial coils. These coil locations are set a-priori based on the subject's MRI and so there is no ambiguity in co-registration. Initial results based upon 10 recording sessions, each of 10 minutes duration, show standard deviations of nasion, left and right pre-auricular coils of 0.43, 0.29 and 0.48 mm respectively with maximum deviation from mean position for the nasion coil of 0.93mm in the vertical axis. These results highlight the utility of this new generation of headcasts in MEG experiments in which high spatial accuracy is required. Simulations (Troebinger et al. 2014) suggest that this level of coregistration noise will increase the sensor level SNR of a typical MEG recording by a factor of 5. These results suggest that this new generation of headcast will allow us to make use of precise anatomical models and to build up very high SNR datasets.

Troebinger L, López JD, Lutti A, Bradbury D, Bestmann S, Barnes G. High precision anatomy for MEG. Neuroimage. 2014;86:583-91.

P4-094

CORTICAL AUDITORY ACTIVITY IN PEOPLE WITH COCHLEAR IMPLANTS: A PRELIMINARY MEG STUDY.

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Hearing in deaf people can be restored with a cochlear implant (CI), an electronic device which transforms the acoustic signal into an electrical pulse, directly stimulating the fibers of the acoustic nerve. Neuroplasticity has been found even in adult brains after implantation. However, the neuronal correlates of the reorganization of auditory cortex during rehabilitation remain unclear. Non-invasive neuroimaging techniques can be used to study brain reorganization after CI. MEG seems the most appropriate method in terms of temporal and spatial resolution, comfort and safety but because CI introduces considerable noise, it has not been widely used.

The aim of this study was to characterize how cortical activity might be confounded by the presence of a CI during a MEG measurement.

Normal hearing subjects were asked to perform a simple auditory experiment, with and without a cochlear implant placed on the left ear mastoid, inside an Elekta Neuromag Vectorview system with 306 channels (204 gradiometers and 102 magnetometers). In the experiment with the CI, the superconducting quantum interference devices (SQUID) were not damaged. One third of the channels, mostly magnetometers localized on the CI side, were saturated and manually excluded from the data. The rest of the analysis pipeline was applied to both datasets (with and without CI): Event-related fields (ERF) were calculated and localized using a Linear Constrained Minimum Variance (LCMV) beamformer algorithm.

The results prove that a CI can be used inside the MEG. Although the electrical current generated by the device produces a strong artifact, this can be eliminated by removing noisy sensors. Furthermore, cortical auditory activity can be detected by evoked response using spatial filters. The results, which can easily be replicated in a clinical population, demonstrate the viability of future longitudinal studies on how cochlear implantation affects neuroplasticity and brain reorganization in deaf people.

P4-095

APPLICATION OF MULTIPLE EQUIVALENT CURRENT DIPOLE MODELING FOR ANALYZING MAGNETOENCEPHALOGRAPHY ACTIVITIES IN A PATIENT WITH AN ATYPICAL FORM OF BENIGN FOCAL EPILEPSY OF CHILDHOOD

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Object: To provide new insight on the location and propagation of the unusual brain activities observed in patients with benign focal epilepsy of childhood using magnetoencephalography (MEG).

Methods: A 7 year old girl presented after a single nocturnal episode characterized by whole body stiffening, extension of all four limbs, and jerking. This was accompanied by her eyes rolling up and unresponsiveness that lasted several minutes. Electroencephalography (EEG) showed sharp waves with stereotyped diphasic morphology and a complex dipolar distribution, manifesting maximum negativity in the frontal region and lower amplitude positivity in the ipsilateral parietal region. The sharp waves were abundant during light sleep, at times occurring in runs. These EEG features are consistent with an unusual form of benign focal epilepsy of childhood. Indeed the patient is neurologically normal and seizure free without medications at 1 year follow up.

Interictal activities were not amenable to simple localization using a single equivalent current dipole (ECD) model because there were two regions (frontal and parietal) activated simultaneously. Accordingly, multiple ECD modeling was applied to analyze the interaction of these two activities during simultaneous MEG / EEG recording.

Results: Multiple ECD modeling revealed activities arising from the parietal region, propagating to the ipsilateral frontal region, and returning to the parietal region, thereby explaining the complicated EEG pattern of frontal negativity and parietal positivity. The orientations of the first and the third dipole components in the parietal region were orthogonal. Therefore, this type of modeling suggests that the epileptic activity in the parietal region evolves from a single ECD into a "regional (rotating)" source.

Conclusion: Magnetoencephalographic recording, coupled with multiple ECD modeling, helps to clarify the complicated brain activities seen in this atypical form of benign focal epilepsy of childhood, and provides further insight into the complexity and proper interpretation of scalp EEG recordings.

P4-096

DYNAMIC STATISTICAL PARAMETRIC MAPPING (DSPM) FOR FOCAL CORTICAL DYSPLASIA (FCD) AT BOTTOM OF SULCUS

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Equivalent current dipoles (ECD) fitted to interictal spikes recoded using MEG tend to cluster or scatter in regions adjacent focal cortical dysplasias (FCD) when these lesions are located at the bottom of a sulcus (BOS). Dynamic statistical parametric mapping (dSPM) can be used to overlay spatiotemporal distributions of spike sources of MEG onto inflated brain model. We hypothesize that dSPM delineates spike activation from FCD at the BOS with better spatial accuracy than ECD.

We collected 4 patients with FCD type II at the BOS. We compared dSPM for 100 ms surrounding MEG spikes with ECDs using a single ECD model. We reviewed spatial congruence between clustered ECDs and FCD. We set a threshold of spike activation (SA) of dSPM with a significance of p<0.0001 from the background magnetic field. The maximum spike was defined on a sensor channel with the largest SA close to the FCD. We defined a leading spike as a significant dSPM SA between trough and the peak of the maximum spike. We evaluated correlations between significant SA areas and FCD.

The volume of FCD ranged from 2255 to 4707 mm3. The depth ranged from 23 to 33 mm. We analyzed 246 MEG spikes for the ECD model and 240 MEG spikes for dSPM. DSPM collected 85 significant SAs including 50 leading spikes in FCD.

Three patients presented 12, 116 and 78 ECDs in each cluster with FCD volumes of 2255 mm3, 3351 mm3 and 4707 mm3. ECDs were partially concordant, with less than 50 % overlapping the FCD lesion. Significant SA identified using dSPM localized to the FCD for 10/10(100%), 10/14(71%) and 27/48 (56%) interictal spikes in three patients, respectively. The remaining one patient presented 22 ECDs in a cluster which was discordant with FCD (volume, 2669 mm3). DSPM showed significant SA in FCD in 3/13(23%) for this patient.

DSPM may delineate spike activations generated from FCDs with small volumes located at the BOS and may show performance to the FCD method in these cases.

P4-097

OPTIMISING BEAMFORMER REGIONS OF INTEREST ANALYSIS

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The computation of a location specific beamformer filter depends solely on an estimate of the data covariance matrix and on the forward model. Increasing the number of M/EEG sensors, increases the quantity of data required for accurate covariance matrix estimation. We show how temporal (Bayesian Principal Component Analysis - bPCA) and spatial (lead field projection) methods can be combined to effectively reduce the number of sensors and optimally represent sources within a region of interest (ROI). Combining these approaches results in enhanced beamformer performance for an ROI for relatively short time windows.

For simulated MEG data combining a spatial projection with bPCA allowed accurate determination of the true dimensionality (the number of sources) of the data. Furthermore, In a realistic simulation with 75 sources, an improvement an improvement in source estimation for a single source of interest was achieved by our proposed approach across a range of signal-to-noise levels and time windows for covariance matrix computation. Finally we illustrate the utility of the approach for the analysis of noisy data collected from a Parkinsonian patient with intracranial DBS (Deep Brain Stimulation) electrodes in the subthalamic nucleus (STN). Based on a prior hypothesis about increased motor cortical-subthalamic nucleus coupling in the beta band in Parkinson's disease an ROI was constructed around the primary motor cortex (M1). Our proposed approach resulted in a more focal topography of STN-cortical coherence and an increased peak t-statistic at the single subject level.

The choice of an anatomical ROI prior to source estimation has a number of benefits. In addition to excluding uninteresting variance or noise from other regions the brain (or environment), it reduces the effective signal space (decreasing the effective number of channels) and therefore improves the estimate of data covariance. This translates in practice to better artefact immunity and more accurate source reconstruction.

P4-098

SOURCE RECONSTRUCTION OF SLOW AND FAST SLEEP SPINDLES USING A BEAMFORMER APPROACH – A MEG/EEG STUDY

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Introduction: Human sleep presents with fast and slow sleep spindles, which differ in frequency and topography. While fast spindles are related to memory consolidation and are modulated by the slow oscillation, less is known about slow spindles. We applied MEG to identify each spindle type's neuronal source.

Methods: We recorded simultaneous EEG and electromagnetic activity, using a whole-head MEG with 275 axial gradiometers (CTF MEG Systems, Port Coquitlam, Canada), from 6 subjects in supine position. Out of six participants two achieved stable light (N2: 48/34min) and deep (N3: 24/64min) sleep. Slow (n=91/63) and fast spindles (n=155/449) were detected in the EEG (Fz, C3) using an algorithm.

We then characterized slow (11+-1 Hz) and fast (14+-1 Hz) spindle-related MEG activity. MEG spindle sources were localized by beamforming, using an adaptive spatial filtering technique (Gross et al., 2001) implemented in FieldTrip. The sources were localized contrasting MEG activity around EEG-defined spindle peaks (+-400ms) to non-spindling periods.

Results: Slow spindles were associated with medial frontal sources [-2 44 -18] whereas fast spindles had parieto-occipital sources [-22 -60 20]. Furthermore, one of the subjects had a widespread source in the temporal lobe [-52 6 -36] when directly contrasting the fast spindle versus the slow spindle type.

Discussion: We demonstrated that sleep spindles can be localized using MEG. Importantly, slow and fast spindles are associated with frontal and posterior areas, respectively. Similar to previous reports (Anderer et al. 2001, Manshanden et al., 2002) we find fast spindles to be produced in parieto-occipital regions as well as temporal cortex (cf. Dehghani et al., 2010). It remains to be assessed whether MEG identified sleep spindles would reveal similar sources, since they were reported being more discrete and asynchronous (e.g., Dehghani et al., 2010).

P4-099

INFORMATION CONTENT IN MEG RECORDINGS: COMPARING LOW- AND HIGH-*TC* SQUID ARRAYS

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We compare two superconducting quantum interference device (SQUID) arrays for magnetoencephalography (MEG): one based on low critical-temperature (low-*Tc*) SQUIDs, the other on high-*Tc* SQUIDs [1]. We use Shannon's measure of information transmission through noisy channels, a simple metric that resolves the challenges associated with differing array geometries [2, 3].

The arrays compared herein differed with respect to scalp-to-sensor distance, sensor size (and therefore the number of channels), and sensitivity/noise levels. For the low-*Tc* case, we optimistically estimated the average scalp-to-sensor standoff distance at 20 mm. This parameter was 1 mm for the high-*Tc* case because this is reasonably achievable for high-*Tc* SQUIDs [4]; see the table for other parameters used. Channels were generated via orthogonalization of the lead fields [2].

The results indicate that the high-*Tc* SQUID array, due to its proximity, extracts at least 40% more information than the low-*Tc* one. This extra information suggests high-*Tc* SQUIDs are a promising technology for improving MEG recordings.

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P4-100

HYPER-PARAMETER TYING: A NOVEL METHOD OF CONTROLLING THE SPARSITY IN SPARSE BAYES SOURCE IMAGING (CHAMPAGNE) ALGORITHM

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The sparse Bayes source imaging (Champagne) algorithm has proven to be effective for neuromagnetic imaging [1]. It is robust to various types of noise and interferences, and it can reconstruct multiple sources, even when they are highly correlated [2]. The method produces sparse solutions because a sparsity constraint is integrated in its cost function. However, there are some occasions where the sparsity constraint rather leads to wrong solutions. One such occasion is the estimation of voxel source orientations. In the Champagne algorithm, when the voxel source orientation is known, a diagonal covariance matrix can be used for the Gaussian prior distribution, and this leads to a simple and efficient algorithm. When the voxel source orientation is unknown, a block-diagonal covariance matrix must be used, which prevents the sparsity constraint from being imposed on each component of a source vector. However, the use of such a non-diagonal covariance matrix leads to an algorithm that is significantly complex and computationally expensive, compared to the algorithm for a diagonal covariance matrix. In this paper, we propose a simple method to overcome this difficulty, called the hyper-parameter tying. The proposed method can use a diagonal covariance matrix even when the source orientation is unknown. However, in each step of the updating iteration, the source variance parameters of vector components are tied together to correctly estimate the source orientation. Since a diagonal covariance matrix is used, the algorithm keeps the simplicity and computational efficiency. We discuss why the hyper-parameter tying can control the sparsity by presenting the cost function analysis of the Champagne algorithm.

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P4-101

BAYESIAN MULTI-DIPOLE ESTIMATION IN TIME AND FREQUENCY WITH MONTE CARLO SAMPLERS

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We present a novel Bayesian method for multi-dipole estimation [1], that can be thought of as a generalized multi-dipole fitting: one can select either a

single time point or a whole temporal window, and the method provides the posterior probability distribution for the number of sources, for the dipole locations and (when the input is a time series) the source waveforms. The very same method can be used to analyze data in the frequency domain, by feeding the algorithm with the (complex) Fourier transform at a selected frequency or frequency band.

The method works as a sequential Monte Carlo sampler [2], where a sequence of distributions is built that transits smoothly from the prior density to the posterior. The computational cost is kept relatively low by marginalizing over the dipole moments, so that only the number of dipoles and the dipole locations are actually sampled.

We show exemplar applications both in the time and in the frequency domain. In the time domain, we analyze the brain response to auditory and somatosensory stimulation, and show the posterior estimates obtained either from a single time point and from a time window, together with the source waveforms. In the frequency domain we consider an eyes open / eyes closed paradigm and present dipole localization of the alpha rhythm.

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P4-102
A COMPUTATIONALLY LIGHT FOUR-SHELL BOUNDARY-ELEMENT FORWARD MODEL FOR MEG

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MEG source imaging is typically carried out using a realistically-shaped three- or single-shell or a sphere-based head model. These models omit the well-conducting cerebrospinal fluid (CSF). In this work, we present a four-shell boundary-element (BEM) model that can be built using freely-available software and that does not add the computational burden of MEG processing.

We generated boundary meshes based on data published as part of the SimNIBS package. The mesh generation was based on an automated pipeline utilizing T1 and T2 MRI data as described by Windhoff et al., HBM 2013. For post-processing, we used surface smoothing from FreeSurfer. Then, we resampled the pial surface to various densities (from 31000 to 5000 vertices) using iso2mesh toolbox; other surfaces were resampled as well. The reference model was built using the densest meshes (44000 vertices) and the Galerkin BEM, and test models were built using the coarser meshes and both Galerkin and collocation BEMs. Then, lead field matrices for 10000 dipoles were constructed and lead-field topographies were compared using relative error RE and correlation coefficient CC metrics.

The results were logical, with median RE increasing from 3% to 8% as the density of pial mesh was decreased from 15000 to 5000 vertices (10th percentiles between 1% and 3%, 90th percentiles between 6% and 17%). The largest errors occurred with weakest sources. The errors were mostly of amplitude nature: 10th and 90th percentiles of CC were between 0.999 and 0.995 and 1.000 and 0.999, respectively. The density of other meshes and, surprisingly, the choice of BEM approach played no significant role.

Our results show that a MEG model containing the CSF can be implemented without excessive numerical burden: a reasonably accurate four-shell collocation BEM model for source-imaging can be built in less than 10 minutes of computation time on a desktop computer.

P4-103
A NOVEL METHOD FOR REMOVAL OF DEEP BRAIN STIMULATION ARTIFACT FROM ELECTROENCEPHALOGRAPHY

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Deep brain stimulation (DBS) has treatment efficacy in neurological and psychiatric disorders such as Parkinson's disease and major depression. Electroencephalography (EEG) is a versatile neurophysiological tool that can be used to better understand DBS treatment mechanisms. DBS causes artifacts in EEG recordings that preclude meaningful neurophysiological activity from being quantified during stimulation. To avoid stimulus artifacts, previous EEG studies on DBS subjects have resorted to turning the stimulator off during recording while a few studies have applied a simple low pass filter to study frequencies well below 50 Hz. In this study, we aimed to fully characterize the DBS stimulation artifact and then removed it with matched filters. The approach was validated by using synthetic EEG data with the DBS on, which was created by adding simulated DBS artifact to a known EEG base signal. Mean squared error (MSE) between the original base signal and the recovered signal was used to quantify the effectiveness of the approach. The DBS artifact was accurately characterized by a series of narrow band components at predicted frequencies based on the DBS stimulation and EEG recording setup. The filtering approach successfully removed the DBS artifact with the MSE value being less that 2% of the base signal power for the range of typical stimulation and signal acquisition parameters. General guidelines on how to setup DBS EEG studies and configure the subsequent artifact removal process were described. In summary, this study established a method through which DBS artifact in EEG recordings can be reliably eliminated, thereby preserving a meaningful neurophysiological signal through which to better understand DBS treatment mechanisms.

P4-104
EXTRACTING SPATIOTEMPORAL PATTERNS FROM SPONTANEOUS MEG DATA

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In nonhuman studies, it is reported that spatiotemporal patterns emerging in spontaneous brain activities reflect past experiences embedded in neural

circuits. In human studies, however, spatiotemporal patterns in spontaneous EEG or MEG data have not been examined well. This is because extracting spatiotemporal patterns is difficult owing to their unknown onsets. Here, we propose a method to extract spatiotemporal patterns that appear frequently from spontaneous MEG/EEG data. This method iteratively searches for spatiotemporal patterns and their onsets, with the aim of minimizing the residual error between the observed and reconstructed data. We tested the performance of this method using real MEG data. From continuous MEG data during a visual stimulation task, this method extracted a spatiotemporal pattern resembling a visual evoked response without using stimulus onset information. This result confirms the applicability of the method for real MEG data. By applying this method, it will be possible to examine how past experiences are engraved in our brains from spontaneous MEG/EEG data.

P4-105

TRANSCRANIAL MAGNETIC STIMULATION WITH ADJUSTABLE PENETRATION DEPTH USING MULTIPLE COAXIAL CIRCULAR COILS

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Transcranial magnetic stimulation (TMS) is a technique for noninvasive stimulation of the human brain. Stimulation is produced by generating a brief, transient high intensity magnetic field by passing a brief, transient electric current through a magnetic coil placed upon the scalp. As a noninvasive method to stimulate brain, TMS has attracted considerable interests as an important tool for studying the functional organization of the human brain as well as a therapeutic tool to improve psychiatric disease.

Stimulation of deeper brain structures by transcranial magnetic stimulation (TMS) plays a role in the study of reward and motivation mechanisms, which may be beneficial in the treatment of several neurological and psychiatric disorders. In the past decade, several coil configures such as double-cone and H-coils have been developed for deep transcranial magnetic stimulation (dTMS). However, the ability of either double-cone coil or H-coil to stimulate deeper brain structures is obtained at the cost of poor stimulation focality.

This paper presents a new coil design for dTMS with adjustable penetration depth by employing three coaxial circular coils with different radius surrounding the head model. The pulse currents with varied amplitude and flowing directions were fed into each of the coils. Three-dimensional distributions of the magnetic fields and induced electric fields in spherical head model with five concentric spheres as well as in realistic head model were calculated by employing impedance method. The electrical properties of head tissues are modeled using the 4-Cole-Cole method. Simulation results show that the coil design in this paper provides a flexible way to produce penetrating electric fields with improved focality in deep brain regions with less fields in superficial cortical tissues.

P4-106

MEG/EEG MAP TOPOGRAPHY AND SOURCE DISTRIBUTION ANALYSIS ON THE EPOCH LEVEL BY NON-PARAMETRIC RANDOMIZATION TESTS

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In Event-Related Field (ERF) and Event-Related Potential (ERP) experiments, stimuli are presented repeatedly, and the subject's brain response is recorded using MEG or EEG, respectively. After artifact removal, epoching, and averaging, though, it is no longer possible to establish whether and for which latencies the averaged waveforms are significantly different between stimulus types, nor whether the epochs per stimulus type are consistent enough to warrant averaging them in the first place. A statistical analysis across epochs can provide exactly this information.

Traditional statistical measures in channel space such as the t-test make disputable assumptions regarding repeatability and independence. Therefore, non-parametric methods have recently attracted attention for the analysis of ERFs and ERPs.

In this contribution, a framework is proposed that allows the application of non-parametric methods such as Topographic Analysis of Variance (TANOVA) and Statistical non-Parametric Mapping of Current Density Reconstructions (CDR SnPM) not only to individual averages in the context of a group study but to the individual epochs themselves, even for single-subject data. Unlike described in previous publications, the statistical analysis is conducted sample-by-sample as opposed to using a maximum statistic over all samples. The then necessary multiple comparison correction is based on the spectral properties of the data. For CDR SnPM, in addition to a test for significant differences between conditions, a within-condition consistency test is used to justify testing for differences on a sample-by-sample basis.

A Mismatch Negativity (MMN) experiment is used to demonstrate the methods. Latencies and brain locations where the brain response differs significantly between stimulus types are consistent with what is known about the MMN.

P4-107

MAXIMIZING THE INDEPENDENCE OF MULTIPLE ROI ANALYSIS WITH CROIS

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Neuroscientists often want to extract time-resolved data from circumscribed Regions of Interest (ROIs) within the brain that they believe to be involved in their MEEG experiment. A common approach is to estimate activity at all source locations (vertices) using a distributed inverse method, and then simply average those estimates across the vertices within each ROI. However,

this approach does not take into account the point-spread/cross-talk issues associated with ill-posed linear inverse methods. We propose a modified method for extracting data from multiple ROIs, which utilizes information about the PSF associated within a specific inverse operator, in order to minimize cross-talk between each ROI: Cross-talk Region Of Interest Selection (CROIS). An important assumption here is that these are the only ROIs that are truly active; but this assumption is nearly always implicit in ROI-based analyses. Somewhat counter-intuitively, the new method entails averaging data over vertices that are not necessarily within any of the ROIs; we call these new collections of vertices "cross-talk ROIs" (cROIs). We use simulations and real data to show how the data from cROIs suffer from less cross-talk than the more conventional ROI approach. This technique maximizes the independence of the data extracted from source localized data. Simulations provide compelling evidence that CROIS would outperform a standard ROI approach to data extraction. Moreover, the baseline period of activity in a psychological experiment was used to compare how CROIS versus ROI extraction would affect correlations between regions, and CROIS outperformed ROI extraction in all of these tests. In addition to providing a way to avoid false correlations (caused by crosstalk), this work provides a simple way for researchers to at least evaluate the risk of these false correlations.

P4-108
"MAGNETIC FIELD CAMERA" FOR RECORDING SPATIALLY-RESOLVED MAGNETORELAXATION (MRX) OF SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES (SPIONS)

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The spatially resolved quantitative detection of magnetic nano-tracers is a rapidly evolving field of research in material science and biomedical applications as well as in fundamental studies of magnetic material properties.

Our approach to the imaging of SPIONs is based on optically detected magnetic resonance in Cs vapour that is confined, together with an inert buffer gas, in a cubic glass cell. Optical pumping by resonant laser radiation prepares a sub-mm thick layer of spin-polarized Cs atoms. The laser-induced fluorescence emitted by the layer depends on the magnitude and orientation of the local magnetic field. Two-dimensional field distributions are thereby encoded into fluorescence patterns, recorded by a CCD camera. The method allows recording of individual field components of the inhomogeneous magnetic field produced by a nearby spatial distribution of SPIONs. In combination with a flexible choice of the induced SPIONs' magnetization direction, the technique provides valuable input for source reconstruction.

We present field maps from a 23×23 mm2 image plane produced by structured SPION patterns magnetized by a magnetic field pulse. The signal decay following the excitation pulse reflects the magnetorelaxation process. We see no major obstacle for upscaling the sensor size to several cm2, thus allowing the study of tissue samples or small organs/organisms/animals.

Based on the diffusion length of the sensor atoms in the buffer gas we estimate a sub-mm spatial resolution in the imaging plane. The accuracy of the method is currently limited by the design of the magnetization coil and environmental field fluctuations. The current magnetometric sensitivity on the order of 1 nT can be lowered to the 10 pT range in a magnetically more quiet environment.

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P4-109
INFLUENCE OF REALISTIC HEAD MODELING ON THE EEG FORWARD SOLUTION

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The accuracy in solving the inverse problem of EEG heavily depends on the exact simulation of the forward problem. Therefore, a detailed modeling of the human head is needed. The goal of our study is to systematically evaluate and compare the influence of modeling the head compartments skin, skull compacta, skull spongiosa, cerebrospinal fluid (CSF), brain grey (GM) and white matter (WM), in order to identify the most important modeling steps, find the most affected brain regions and relate these effects to the numerical error. We therefore created two highly realistic six compartment tetrahedral finite element head models including WM anisotropy - one with a standard and one with a high resolution that will be used as reference. We furthermore automatically generated a simplified hexahedral five compartment head model using FieldTrip-SimBio (fieldtriptoolbox.org/development/simbio). Starting from a three compartment scenario (skin, skull, brain), we subsequently refine the standard resolution head model by distinguishing one further compartment. For each of the generated five head models, we measure the effect on signal topography and magnitude both in relation to the reference model and to the previous refinement step. Comparing the fully detailed standard resolution model to the reference model allows us to estimate the numerical error. Our results show that CSF and GM/WM should be distinguished in a realistic head model, while the additional distinction of skull compacta/spongiosa has a comparatively weak effect when using an optimized conductivity value.

The inclusion of anisotropic WM leads to effects that are nearly as big as those for CSF and GM/WM distinction, but also to an increased workload in model generation. The use of an automatically generated five compartment head model leads to a reasonable simulation accuracy when considering the clearly reduced work effort.

P4-110
USING SPARSE CLASSIFICATION IN SOURCE SPACE TO REVEAL PATTERNS OF DIFFERENT ACTIVATION DURING CATEGORY PERCEPTION IN THE MEG

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The categorization of different stimuli is a vital function of the human brain. The statistical significance of differences in EEG/MEG activity between two categories is mainly assessed using univariate methods. These approaches, however, miss effects that are not confined to one particular location in time, frequency and space. Multivariate classification methods are a promising route to overcoming this limitation by identifying global patterns characterizing a cognitive state.

17 participants (10 male; age 28 ± 8; all right handed) were presented with 40 grayscale images of faces and bodies each for 750ms, followed by an ISI of 1700±300ms while MEG was acquired at 1000Hz. Each time-frequency-bin of the wavelet transformed data (5-20Hz; 0-500ms; Δt=50ms) was projected into source space using an individual DICS filter. We used a 5 fold cross-validated Elastic Net Classifier with high sparsity constraint (α= 0.005) on each subject. Above chance performance for mean accuracies was tested using a one-sided t-test and validated using the Bayes factor (B_10).

On average, our classifier performed above chance level ($p < 0.004$; B_10 = 2.5). Informative regions included primary visual regions at 0-200ms post stimulus covering the alpha and beta range and right fusiform areas at ~500ms post stimulus in the alpha band. The detected pattern also included parietal and pre frontal regions. Using an uncorrected t-test, the occipital and fusiform effects can be reproduced but neither survives correction. A ROI analysis would show the occipital and fusiform effects but miss the parietal and pre frontal ones.

Multivariate classification methods can decode complex categories in source space. Our findings not only replicate previously reported areas from neuroimaging studies, but also extend these by showing the involvement of more widespread activity in time, space and frequency.

P4-111
MOMENTARY-UNCORRELATED COMPONENT ANALYSIS, MUCA, FOR BLIND SOURCE SEPARATION OF EVOKED EEG/MEG DATA

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Momentary-uncorrelated component analysis (MUCA) is a novel tool designed for blind source separation (BSS) of latent source components underlying non-stationary multi-trial EEG/MEG data. The separation of the latent components is based on utilizing the changing second-order statistics in the evoked data by joint diagonalizing multiple estimated covariance matrices.

The input data for the method are the momentary covariance matrices (MCMs) computed over the trials at each time instant after the stimulus. Because of non-stationarity of the data, the collected MCMs provide complementary information for MUCA. It is possible to reduce noise substantially by linearly manipulating the MCMs since the latent components remain uncorrelated also after such operations. The task is then to find an unmixing matrix that optimally diagonalizes all the preprocessed MCMs thus revealing covariance matrices that represent the latent components. Several computational joint diagonalization methods are possible for this purpose. The resulting unmixing matrix can separate the measurement data into the latent components.

MUCA was compared with independent component analysis algorithm FastICA. The independence assumption is stricter than uncorrelatedness and more difficult to implement and test afterwards. We tested MUCA using simulated data and measured TMS-evoked EEG and compared the results with those from FastICA.

The simulation results show that both MUCA and FastICA are capable of uncovering simulated latent components. However, MUCA is distinctly more robust with respect to difficulties in the data, e.g., noise and high number of components. In the analysis of the measured data, both methods can find reasonable components, which partly correspond to each other.

Overall, as a robust BSS method, MUCA is highly useful in interpreting the structure of complex EEG, since timing and localization information is simpler and more accurate to infer in a single component than in the original data.

P4-112
NOVEL METHODS FOR IMPROVING SOURCE LOCALIZATION USING HYBRID ULTRA-LOW-FIELD MRI AND MEG

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As a functional brain imaging modality, magnetoencephalography (MEG) surpasses functional magnetic resonance imaging (fMRI) in terms of temporal resolution and has a spatial accuracy superior to electroencephalography (EEG). However, the spatial accuracy is limited by coregistration, the procedure of aligning a structural image of the head with the MEG coordinate system. Coregistration contains errors produced by a number of factors, such as the head-position measurement in MEG and the identification of anatomical landmarks in both MEG and structural MRI. Errors are also caused by MRI distortions, skin movements and small differences between supine and seated positions regarding the geometry of the soft brain and cerebrospinal fluid. Further, as models for source localization become more detailed, their sensitivity to inaccuracies in geometry and conductivity values increases. The volume currents being especially important in EEG, an accurate model of the

conductivity structure is also needed to obtain full benefit of the complementary information of simultaneous EEG and MEG. A hybrid MEG-MRI system provides natural approaches to addressing these issues.

SQUID sensors tailored for ultra-low-field (ULF) MRI can also be used for MEG. We show that, together with high-precision ULF-MRI electronics and a stable coil structure, the common sensor array can be used to transform the largely manual coregistration problem to a fully automatic calibration, thereby eliminating human error. We further discuss the unique possibilities, shown recently, of ULF MRI in current-density imaging (CDI), potentially allowing also the imaging of electrical conductivity using the same hybrid device. We describe our methods, computations, and experimental setups for implementing the methods in our hybrid MEG-MRI system at Aalto University, along with preliminary results. If successful, conductivity imaging combined with sub-millimeter automatic coregistration provides significant improvements to MEG and EEG source localization.

P4-113
MAGNETRODES PROJECT: SENSING THE MAGNETIC FIELD OF NEURONS AT LOCAL SCALE

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“Magnetrodes” is a European project whose main goal is to develop a new generation of tools for electromagnetic recordings and spectroscopy at the neuron level.

Spin electronics offers nowadays the possibility to create very sensitive, micrometer-scale magnetic field detectors. We propose to exploit this technological advance to create novel tools for probing neuronal magnetic fields at the cellular level. The first goal of the project will be to develop the magnetic equivalent of an electrode, a ‘magnetrode’, sensitive enough to detect the very small magnetic fields induced by the ionic currents flowing within electrically active neurons, and small enough to probe a limited number of cells. We will adapt magnetrodes also for local nuclear magnetic resonance spectroscopy (MRS); thus, these probes could record both electromagnetic and chemical activity of neurons. In addition, means for local electric or magnetic stimulation will be integrated into magnetrodes.

We will develop magnetrodes for in-vitro and in-vivo measurements at various spatial scales, from brain areas down to single neurons. In parallel, based on the measurements with magnetrodes, we will augment existing computational models and develop new ones to characterize the electromagnetic fields emitted by neurons and assemblies of neurons. We will employ these models to bridge from the activity of single neurons to macroscopic non-invasive measurements such as electroencephalography (EEG) and magnetoencephalography (MEG).

Here, we will describe the first probes that have been fabricated for the in-vitro and in-vivo experiments, illustrate initial results and discuss the potential of the project.

Satellite

SATELLITE 1: "ZERO TO HERO": AN OVERVIEW OF MEG DATA ACQUISITION, ANALYSIS AND INTERPRETATION

CHAIRS:

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With the MEG field expanding rapidly it is critically important that new researchers have the opportunity to learn from established scientists. The purpose of this educational satellite is to give a complete overview of MEG, including data collection, analysis and interpretation. Such an in-depth knowledge, spanning SQUIDs all the way up to advanced analyses is key, if MEG is to realise its potential as a tool for basic neuro-scientific and clinical study. By the end of this satellite, attendees should have a good understanding of:

i) The fundamentals of the MEG system including SQUIDs, pick up coils, cryogenics, and advanced strategies for interference rejection
ii) The principle techniques used for analysing MEG data in source space, including state of the art techniques for solving the MEG forward and inverse problems as well as connectivity analysis and statistical testing.
iii) How to set MEG in the context of other brain imaging modalities and neuroscience findings. This will include the latest findings in the study of event related fields, neural oscillations and generative models

SATELLITE 2: BIOMAGNETIC SIGNAL PROCESSING: DENOISING, SOURCE LOCALIZATION, AND CONNECTIVITY ANALYSIS

CHAIRS:

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SEKIHARA, Kensuke, Tokyo Metropolitan University, Tokyo, Japan, k-sekihara@nifty.com

In this satellite meeting, leading scientists provide talks on their cutting-edge methodology on biomagnetic signal processing. Their talks are designed to be a graduate-student level; namely, the speakers intend to provide their explanation, assuming that the audience includes students or newcomers to the MEG field. This satellite meeting provides a friendly atmosphere for discussion and exchange of ideas for the expert audience and an educational opportunity for students.

This satellite meeting will cover topics ranging from signal analysis of MEG sensor data including novel oscillatory data analysis methods and cross-frequency coupling analyses. The meeting will also have several talks on novel source localization algorithms and talks that examine properties of spatial resolution of MEG. Finally, many talks will focus on novel methods for functional connectivity and network analyses.

SATELLITE 3: OPEN SOURCE ACADEMIC SOFTWARE FOR BASIC AND ADVANCED MEG ANALYSIS

CHAIR:

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The purpose of this symposium is to familiarize the attendees with the freely available academic software packages for MEG data analysis. This should allow the attendees to make an informed choice among the available tools to jump-start their future MEG analyses.

In this half-day satellite symposium, the MEG/EEG open-source community will demonstrate the capabilities of the software they develop and support. We will give short presentations during which the developers of Brainstorm, FieldTrip, MNE, NutMEG, SPM and SIFT will introduce their packages, focusing on MEG analyses. Commonalities and differences between the packages will be emphasized to inform the users how to select the right tools for their analyses. The interoperability between the packages will be explained. Subsequently, parallel breakout sessions are organized in which the participants are split over small groups to interact closely with the developers, to ask questions and get further hands-on demonstrations.

SATELLITE 4: ULTRALOW FILED MAGNETIC RESONANCE IMAGING

CHAIR:

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Interest in ultralow field magnetic resonance imaging (ULFMRI) is steadily growing, not least because of recent demonstrations of its integration with multichannel systems for magnetoencephalography (MEG). The goal of this satellite is to provide an overview of the current state of the art of ULFMRI. The principal objectives are: (1) to provide the audience with a broad understanding of the basis of ULFMRI, which involves nuclear magnetic resonance, the longitudinal and transverse relaxation times T1 and T2, prepolarization of the protons to enhance the signal, detection with a SQUID, and the principles of frequency and phase encoding to obtain images; (2) to discuss solutions to limitations of ULFMRI caused by transient and environmental magnetic fields; (3) to examine methods of reducing the noise of SQUIDs and other detectors; (4) to present recent results on imaging the brain, including integrating ULFMRI with MEG, measuring current densities, dramatically increasing the contrast between different brain species using novel pulse sequences, and direct detection of long-lived neuronal activity;

(5) measuring and understanding the enhanced tissue contrast available at ULF; (6) perspectives on potential improvements in ULFMRI technology and new applications.

SATELLITE 5: BRAINSTORM COMMUNITY WORKSHOP

CHAIR:

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Brainstorm is a collaborative, open-source application dedicated to MEG/EEG/sEEG/ECoG data analysis (visualization, processing and advanced source modeling). Our objective is to share a comprehensive set of user-friendly tools with the scientific community using MEG/EEG as an experimental technique. For physicians and researchers, the main advantage of Brainstorm stands in its rich and intuitive graphic interface. We are also putting the emphasis on practical aspects of data analysis to promote reproducibility and productivity in MEG/EEG research. Since the project started at the end of the 1990's, our server has registered more than 8,500 accounts and 200 journal articles were published with results obtained using Brainstorm. In 2013, we recorded an average of 500 downloads per month.

This satellite workshop will feature both oral communications from Brainstorm users and a hands-on training course. It is a unique opportunity for the Biomag community to provide feedback on the software, to help its developers improve and provide new features, and to carry in-depth insight about current and future developments to new users.

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